THESIS

FOR THE AWARD OF DEGREE OF

MASTER OF SURGERY (General Surgery)

SESSION 2020-2023

"CHRONIC CALCULUS CHOLECYSTITIS: A CLINICOPATHOLOGICAL STUDY WITH LAB-BASED EVIDENCE"

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SANTOSH DEEMED TO BE UNIVERSITY
NO. 1, SANTOSH NAGAR,
GHAZIABAD-201009, NCR DELHI, INDIA

DEPARTMENT OF GENERAL SURGERY
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ACKNOWLEDGEMENT

"Accept your past without regret

Handle your present with confidence

Face the future without fear"

- Dr .A.P.J Abdul Kalam

Having dreamed big at a young age to be where I am, has been an adventurous journey with both success and failure. Throughout my journey my family, mentors, friends, colleagues have instilled in me the confidence, and motivated me constantly.

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Dr. Janani R. G.
(2020-2021)

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INTRODUCTION

INTRODUCTION

Gallbladder is a pear-shaped saccular organ, which stores bile becomes a place for formation and growth of gallstones. In the west gall stone diseases are more common.[1] Today the incidence of cholelithiasis is increasing considerably in India, possibly due to change in the dietary habits, which is becoming westernized and changing lifestyle.

Cholecystitis is defined as a chemical or bacterial inflammation of the gallbladder and is one of the commonest biliary pathologies. Cholecystitis associated with gallstones is the most common type, occurring in about 90-95% cases.

The aetiology of cholecystitis is multifactorial. Stasis of bile within the gallbladder with consequent maintenance of contact between stagnant bile and the gallbladder wall resulting in chemical irritation is considered as one of the causes of cholecystitis. A bacterial cause of cholecystitis had been proposed with positive bile cultures seen in as many as 35-40 % of cases. Pancreatic juice with its enzymatic properties also acts as an etiological factor in pathogenesis of cholecystitis.

There are several risk factors for the development of calculous cholecystitis of which female gender, obesity; dietary factors play a vital role. The incidence of cholecystitis is higher in females, with a female to male ratio 3:1 up to about the age of 50 and a ratio of approximately 1.5:1. The incidence varies in different parts of the world. In India, the female to male is 4.4:1 by ratio. The prevalence of cholecystitis in the Indian subcontinent also varies in different regions.[2]

Gallstones are described as cholesterol, mixed, and pigment stones.[3] Cholesterol and mixed stones are formed from biliary sludge, due to stasis in the gallbladder. Pigment stones are composed of salts of unconjugated bilirubin, with varying amounts of cholesterol and protein.

The histological features of chronic calculus cholecystitis are as follows:[4]

1. A predominantly mononuclear inflammatory infiltrate in the lamina propria with or without extension to the muscularis and pericholecystic tissues.
2. Fibrosis
3. Metaplastic changes.

However, recurrent episodes of biliary colic may be associated with a scarred, shrunken gallbladder and Rokitansky-Aschoff Sinuses.

Chronic calculous cholecystitis is an inflammatory disease which affects the gallbladder wall and causes dysfunction of the biliary system, accompanied by presence of gallstones in the gallbladder lumen, and reveals as biliary colic. Biliary colic is the most common symptom of cholelithiasis.[5] Approximately 75% of patients visit the hospital due to abdominal pain. Biliary colic is caused by intermittent obstruction of cystic duct by gallstones.

For chronic calculous cholecystitis, ultrasonography is the initial diagnostic study of choice and most of the times it's the only study that is required for the diagnosis of the condition.

The management of chronic calculous cholecystitis includes surgical modality. The surgical management is elective cholecystectomy, either standard open approach or, alternatively laparoscopic cholecystectomy. Laparoscopic cholecystectomy nowadays is the treatment of choice. Various studies have reported that elective cholecystectomy can be performed with death of around 1%.[6]

The recent acceptance of laparoscopic surgery in the management of gallstone disease had expanded the therapeutic options. The expansion of interest in these techniques had been one of the major success stories of biliary surgery in recent years.

Gallbladder disease is very common in Northern India resulting in various morphological patterns, most common of which is chronic cholecystitis. Very rarely eosinophilic cholecystitis can be seen which represents 0.25% to 6.4% of all cholecystitis. It generally presents in the absence of gallbladder stones. Eosinophilic cholecystitis is diagnosed histo pathologically when more than 90% of the cellular infiltrate comprises of eosinophils present transmurally. In cases where eosinophilic infiltrate is 50-75% and other inflammatory cells are also present it is known as lympho-eosinophilic cholecystitis.

Although there are quite a few case reports describing eosinophilic cholecystitis in association with other conditions, the aetiopathogenesis of disease still remains obscure.[7]

Various probable reasons have been reported which include allergies, parasites, eosinophilic enteritis, and local reaction to gall stones. However, if a postoperative histopathological diagnosis of eosinophilic cholecystitis is made, then the patient must be

investigated thoroughly to rule out other associated disease conditions, which may have a worse prognosis than cholecystitis itself.[7]

While reviewing the literature it was found that eosinophilic cholecystitis had mainly been reported as case reports and very few large series study have been done on this entity.

AIMS AND OBJECTIVES

AIMS AND OBJECTIVES

Aim:

The aim of the study is to assess the socio-demographic and clinical profile of chronic calculus cholecystitis cases presenting to the Department of Surgery at Santosh medical college and hospital, Ghaziabad.

Objectives:

1. To study the pattern of age and sex distribution, economic status, diet and clinical feature of patients.
2. To study the laboratory investigations of patients presenting with the associated pathology.
3. To study the radiological investigations of patients presenting with the associated pathology.
4. To study the intraoperative pathological changes of the gall bladder.

REVIEW OF LITERATURE

REVIEW OF LITERATURE

SURGICAL ANATOMY

GALL BLADDER

It is a pear shaped organ, 7-10 cm long with a capacity of 30- 60 ml.[8] It is located in the under surface of liver (gall bladder fossa) on segment IVB and V. It is enclosed within its peritoneal sheath on three sides and, there is no peritoneal covering, on the side attached to liver ,and a fibrous lining known as the cystic plate occupies this space. Gall bladder can be divided into fundus, body, neck, and infundibulum with Hartmann's pouch.

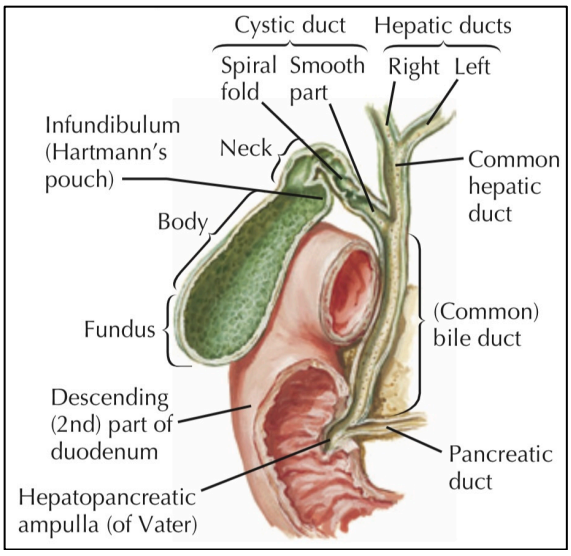


Figure 1:Anatomy of the gall bladder

Fundus

Fundus is the rounded, blind end that normally extends 1 to 2 cm beyond the liver's margin , opposite the upper end of linea semilunaris. Contains the smooth muscles of the gall bladder. A partial folding of fundus may result in 'Phrygian Cap' deformity.[9]

Body

Occupies the gallbladder fossa, covered by peritoneum on 3 surfaces.[10] Main function is storage and contains most of the elastic tissue allowing for distention. Sometimes gallbladder is suspended in a mesentery, off the inferior surface of the liver – wandering gallbladder or rarely embedded deep inside the liver parenchyma - intrahepatic GB.

Infundibulum

It is the angulated posterior portion of the body between the neck and the cystic duct. It may show mucosal outpouching in its medial aspect, called Hartmann's pouch, and is often associated with impaction of stone.

Neck

Neck lies in the deepest part of gall bladder fossa, Neck curves up and forward and then sharping back and downward connecting to the cystic duct. Mucosal lining shows spiral folds give rise to 'spiral valve of heister' and may interfere with the passage of instrument.[10]

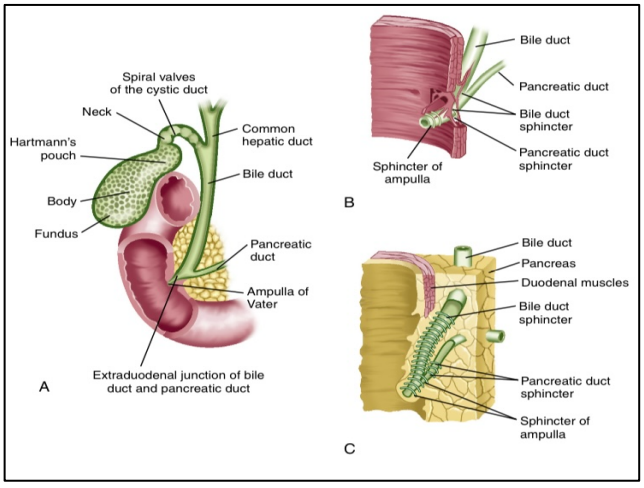


Figure 2: Gall bladder parts

Calot's Triangle

It is also known as cholecystohepatic triangle. The borders of the triangle are – laterally by cystic duct, medically by common hepatic duct and superiorly by the inferior surface of liver. It has the cystic artery and lymph node.

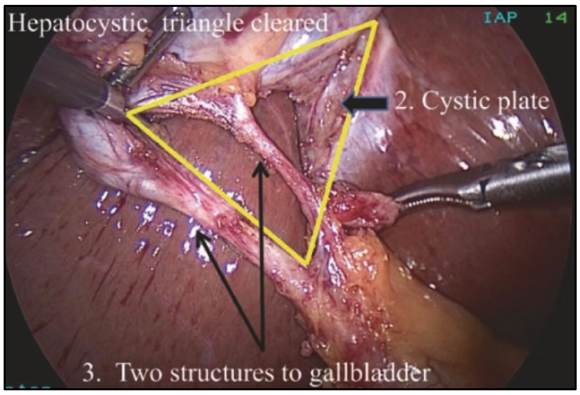


Figure 3:Calot's triangle

Histology

The mucosal lining of the gallbladder is formed by a single, highly redundant, simple columnar epithelium that contains cholesterol and fat globules. The mucus secreted into the gall- bladder originates in tubule-alveolar glands that are found in the mucosal lining of the infundibulum and neck of the gallbladder, but are absent from the body and fundus.

The epithelial lining of the gallbladder is aided by lamina propria. The gallbladder does not have a muscularis mucosa and submucosa. The muscular layer has circular, longitudinal, and oblique fibres. The adventitia has connective tissue, nerves, vessels, lymphatics, and adipocytes. The gallbladder is covered by serosa except where it lies in the liver.

Figure 4:Histology of the gall bladder

Arterial supply

Cystic artery arises usually from the right hepatic artery (>90%), reaches the Gall bladder behind the common hepatic duct and traverses through the hepato-cystic triangle of calot and branches into anterior and posterior branch. The extrahepatic bile ducts are supplied by the right hepatic artery above and gastroduodenal artery below, and the major trunks run along the medial and lateral walls of CBD, sometimes referred to as 3 o' clock and 9'o clock position.[11].

Venous drainage

Venous drainage is carried either through small veins that enter directly into the liver or, rarely, to a large cystic vein that carries blood back to the portal vein. Those from its upper surface lie in the areolar tissue between the gallbladder and liver and usually run directly into the liver through the fossa for the gallbladder to join the hepatic veins. Those from the rest of the gallbladder join to form one or two cystic veins on its neck and these commonly enter the

liver, either directly or after joining with veins draining the hepatic ducts and the upper part of the bile duct. They do not accompany the cystic artery.

Lymphatic drainage

The lymphatic drainage of the gallbladder tends to be considerable and is of major importance for both inflammatory and malignant disease of the gallbladder. The lymphatic channels from the sub-serosal and submucosal plexus drain into the cystic lymph node of Lund, which lies in the fork created by the junction of cystic and common hepatic ducts and to a node situated at the anterior border of epiploic foramen. Efferent vessels from the nodes pass in the free edge of the lesser omentum to the celiac group of pancreatic nodes. The sub-serosal lymphatic vessels of the gallbladder also have connection with the subcapsular lymphatic channels of liver.

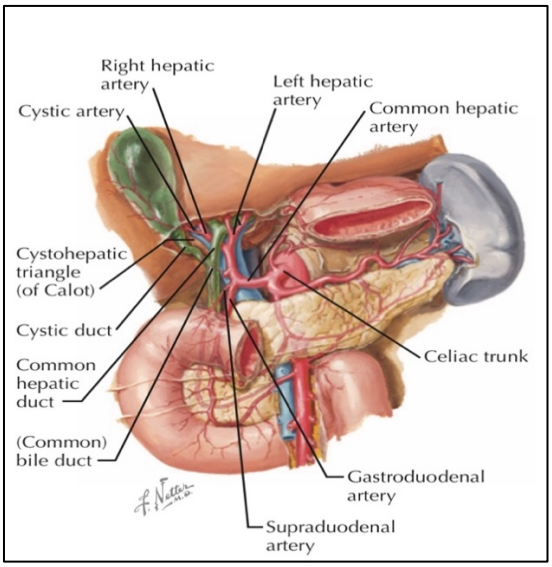


Figure 5:Vascular supply of the gall bladder

Nerve supply

The gallbladder receives parasympathetic, sympathetic and sensory innervation through nerve fibers running largely through the gastro hepatic ligament.

Parasympathetic (cholinergic) fibers arise from the hepatic branches of the vagus nerve to stimulate activity in the gallbladder, bile ducts, and liver. These vagal branches also have peptide-containing nerves containing agents such as substance P, somatostatin, enkephalins, and vasoactive intestinal polypeptide (VIP).

The sympathetic and sensory branches of the gallbladder, liver, and bile ducts pass through the celiac plexus and control gallbladder relaxation and mediate the pain of biliary colic.

EMBRYOLOGY

The hepatic diverticulum comes from the ventral wall of the fore-gut and turns into a stalk to form choledochus. A lateral bud is branched out which become the gallbladder and cystic duct. The embryonic hepatic duct gives out branches which make up the canaliculi in between the liver cells. Normally recanalization subsequently occurs and bile begins to flow. During early fetal life the gallbladder is entirely intra- hepatic.

ANOMALIES

Congenital anomalies of the gall bladder are as follow's:

- The gallbladder can be septate - transversely or longitudinally
- The gallbladder can be a double gall bladder with a single cystic duct.
- The gallbladder may be double with separate ducts opening into hepatic or common or both ducts. The serosa can be separate or common.
- Small ducts may connect gallbladder with liver. Usually these become obliterated. They may persist, which is one of the reasons why drainage is advisable after cholecystectomy.
- The folded fundus (Phrygian cap) deformity is the commonest congenital abnormality of the gallbladder. Is has no pathological significance, but when present it can be seen on cholecystography.
- The gallbladder may have a mesentery: it may be on the left of the falciform ligament, or it may be intrahepatic.

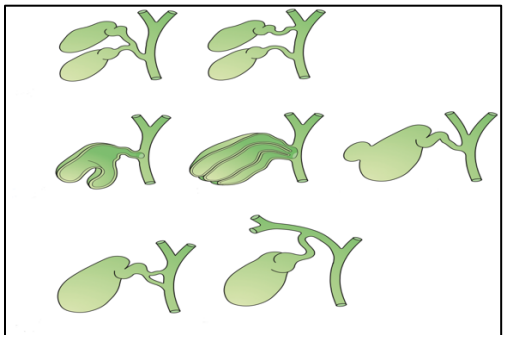


Figure 6: Variations of the gall bladder

Variations of the cystic duct anatomy

- The cystic duct usually joins the common hepatic duct to form the common bile duct within 2-5 cm of the upper border of the duodenum
- Frequently the common hepatic and cystic ducts lie parallel, being joined by connective tissue for some distance before becoming one duct.
- The union of the cystic and common hepatic ducts is frequently behind the duodenum or the pancreas, and occur just before the duct pierces the wall of the duodenum.
- Usually the cystic duct joins the common hepatic duct on its right side. I may, however, join the front, back, or even the left side of the common hepatic by taking a spiral course behind it.
- An accessory bile duct is not uncommon. It is sometimes an accessory right hepatic duct which leaves the right extremity of the porta hepatis, runs down parallel to the cystic duct and behind it, in front of the right hepatic artery, and joins the common hepatic duct anywhere between the site of its formation and the entrance of the cystic duct into the common duct. It is more common to find ducts of varying size goi directly from the liver into the gallbladder.
- The cystic duct may be absent, the common hepatic duct entering the gallbladder and the common bile duct leaving it. It is. perhaps. more accurate to describe the gallbladder in these cases as being sessile. The condition is important, as gall stones can readily enter the common duct.
- A rare anomaly shows the right hepatic duct entering the gallbladder near its junction with the cystic dust. Its surgical importance is considerable. Should it be ligatured, jaundice would result as there is little communication of bile channels between the two parts of the liver drained by right and left hepatic ducts.

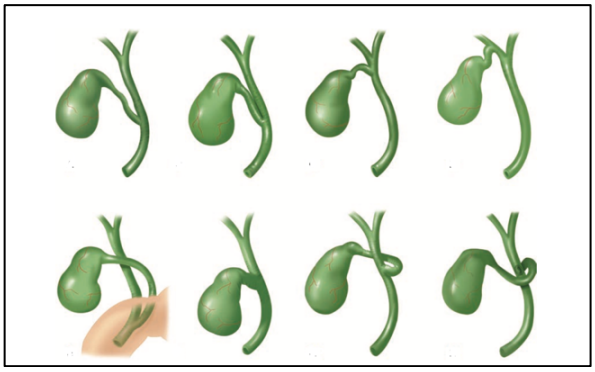


Figure 7: Variations of the cystic duct

Variations of the cystic artery

- The right hepatic artery will go in front of the common hepatic duct.
- The right hepatic artery may lie parallel to and very near the cystic duct and is often behind it.
- The cystic artery may pass in front of the common hepatic duct
- The right hepatic artery comes from the superior mesenteric artery. An accessory cystic artery arises from the right hepatic, left hepatic or some other branch of the hepatic trunk.

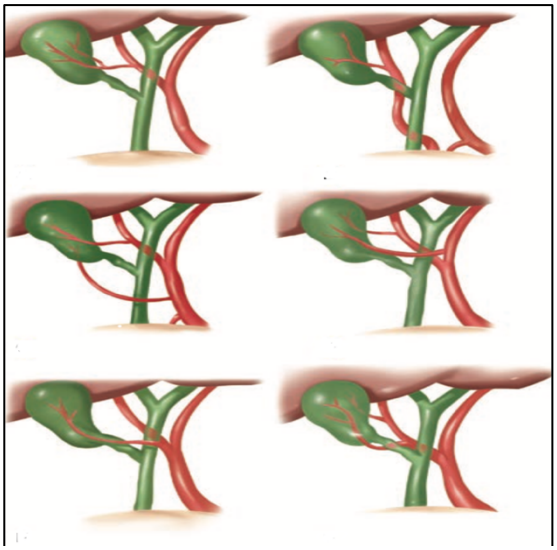


Figure 8: Variations of the cystic artery

BILE DUCTS

The right and left lobes of liver are drained by ducts originating as bile canaliculi in the lobules and these canaliculi empty into the canals of Hering in the interlobular triads and these canals are collected into ducts, and finally come outside the liver as the Right and left hepatic ducts. Right hepatic duct is formed by the union of the anterior and posterior segment ducts of the right lobe of the liver at porta hepatis. The average length of RHD is 0.9 cm.[12] Left hepatic duct is formed by the union of medial and lateral segment ducts of the left lobe of the liver and average length is 1.7 cm – common hepatic duct is formed by union of the right and left hepatic duct and average diameter is about 0.4 cm. Its lower end is defined as its junction with cystic duct.[14]

CYSTIC DUCT

Cystic duct joins the hepatic duct to form the common bile duct. at an angle of about 40 degree.[15] The length of cystic duct is about 2-3 cm in length with a diameter of 3mm. The segment of the cystic duct immediately adjacent to the gall- bladder neck bears a variable number of mucosal folds called the spiral valves of Heister. While they do not have any valvular function, they can make cannulation of the cystic duct difficult. Obstruction of cystic duct leads to hydrops of Gallbladder, contains white bile, composed only of mucus.

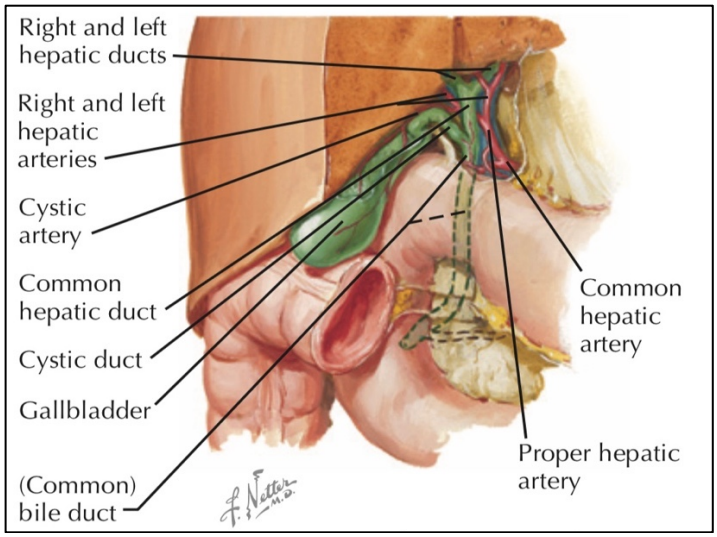


Figure 9: Ductal anatomy

COMMON BILE DUCT

Begins at the confluence of cystic duct and common hepatic duct and ends at the ampula of vater in the second part of the duodenum. This segment is typically about 7 to 11 cm in length and 5 to 10 mm in diameter (average being 6mm), though its diameter can increase slightly with age and following cholecystectomy. CBD is divided into 4 portions- supra duodenal, retro duodenal, pancreatic and intramural.[11]

Supra duodenal portion lies in the right free border of lesser omentum, to the right of the hepatic artery and anterior to the portal vein. Retro duodenal portion descends behind the 1st part of the duodenum and the pancreatic portion tunnel the gland substance. Intramural portion takes an oblique path averaging 1.5 cm though the duodenal wall and receives main pancreatic duct inferiorly. And both of them end in the ampulla of vater on the posteromedial wall of the second part of the duodenum.

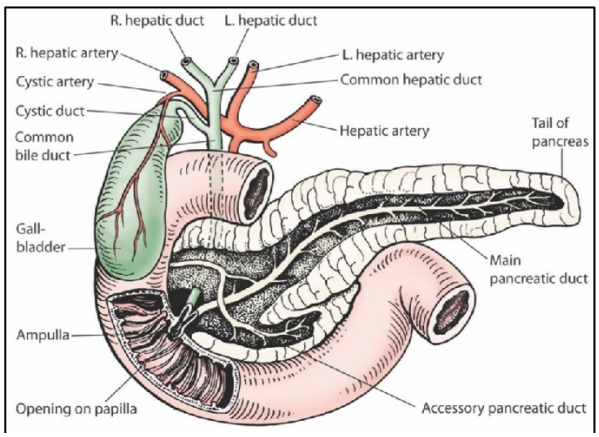


Figure 10: Relations of the gall bladder

PHYSIOLOGY

BILIARY SECRETION

Bile is secreted continuously by the liver cells (hepatocytes) into the biliary canaliculi. Daily secretion of bile is 500 – 1000 ml per day.[13] Bile is secreted at a pressure of 150 – 250mm of water. If obstruction occurs, liver continues to secrete up to the pressure of 300mm of water, after which secretion ceases.[13]

Bile is mainly composed of water, mixed with bile salts and acids, cholesterol, phospholipids (lecithin), proteins, and bilirubin. It also contains several minor components such as electrolytes and vitamins. Sodium, potassium, calcium, and chlorine have the same concentration in bile as in plasma or extracellular fluid. Hepatic bile is usually neutral or slightly alkaline and gallbladder bile is more acidic than hepatic bile.

The primary bile salts, cholate and chenodeoxycholate, are synthesized in the liver from cholesterol metabolism. They are conjugated there with taurine and glycine and act within the bile as anions (bile acids) that are balanced by sodium. These bile acids are then excreted into the bile by hepatocytes .[13]

About 80% of the secreted conjugated bile acids are reabsorbed in the terminal ileum. The remainder is dehydroxylated (deconjugated) by gut bacteria, forming the secondary bile acids deoxycholate and lithocholate. These are absorbed in the colon and can then be transported back to the liver. Eventually, about 95% of the bile acid pool is reabsorbed, the so-

called enterohepatic circulation. Only a small amount (5%) is excreted in the stool, allowing the relatively small quantity of bile acids produced to have maximal effect.

Important functions of bile salts are:

(1) Formation of water soluble complexes with cholesterol, fatty acids and fat soluble vitamins and their absorption.
(2) Reduction of surface tension and emulsification of fat.

Bile salts are powerful choleretic which increases hepatic bile production. Cholesterol and phospholipids synthesized in the liver are the principal lipids found in bile(19). The colour of the bile is due to the presence of the pigment bilirubin (orange or yellow) and its oxidized form, biliverdin (green), which are the metabolic products of the breakdown of hemoglobin, and are present in bile in concentrations 100 times greater than in plasma. Bilirubin conjugated in the liver can be excreted through the urine as urobilinogen (yellow). Remaining excess bile pigment passes into the intestines where bacteria convert it into stercobilinogen (brown), which is excreted through the stool.

FUNCTIONS OF GALLBLADDER

Bile secreted by the liver is stored in the gallbladder. This storage is made possible by the fact that the gallbladder mucosa has the greatest absorptive power per unit area of any structure in the body. It rapidly absorbs sodium, chloride, and water against significant gradients, concentrating the bile as much as 10-fold and leading to a marked change in bile composition. This rapid absorptive capacity is one of the protective mechanisms that prevent a potentially dangerous rise in pressure within the biliary system as bile is produced and stored. In addition, gradual relaxation of the gallbladder as well as routine emptying of the gallbladder's excess bile stores during the fasting period also play a role in maintaining a low resting intraluminal pressure in the biliary tree.

The mucosal cells of the gallbladder secrete two important products into the gallbladder lumen: glycoproteins and hydrogen ions. The mucosal glands in the infundibulum and the neck of the gallbladder secrete mucus glycoproteins that protect the mucosa from the corrosive action of bile and to facilitate the passage of bile through the cystic duct. This same mucus creates the colourless "white bile" seen in hydrops of the gallbladder due to cystic duct

obstruction blocking the entry of bile pigments into the gallbladder. The transport of hydrogen ions plays an important role in decreasing the pH of the stored bile. This acidification helps prevent the precipitation of calcium salts, which can cause stone formation

Bile secretion is under control of neurogenic, humoral, and chemical stimuli. Normal gallbladder filling is facilitated by tonic contraction of the sphincter of Oddi, which creates a small but effective pressure gradient between the bile ducts and the gallbladder. In association with phase II of the inter digestive migrating myenteric motor complex (MMC) in the gut, the gallbladder repeatedly empties small volumes of bile into the duodenum. This process is mediated at least in part by the hormone motilin.

In response to a meal, the gallbladder delivers larger volumes to the intestine by a combination of gallbladder contraction and synchronized sphincter of Oddi relaxation. One of the main stimuli to this coordinated effort of gallbladder emptying is the hormone cholecystokinin (CCK).

CCK is released endogenously from the enteroendocrine cells in the duodenum in response to a meal. When stimulated by eating, the gallbladder empties 50% to 70% of its contents within 30 to 40 minutes. Over the following 60 to 90 minutes, the gallbladder gradually refills as CCK levels drop. Other minor hormonal and neural pathways also are involved in the coordinated action of the gall- bladder and the sphincter of Oddi.

Vagal stimulation increases the secretion of bile, while splanchnic nerve stimulation results in decreased bile flow. Hydrochloric acid, partly digested proteins and fatty acids in the duodenum stimulate the release of secretin from the duodenum that in turn increases bile production and bile flow.[13] Cholecystokinin also increases the hepatic secretion of bile. Hormones such as vasoactive intestinal polypeptide (VIP) and somatostatin are potent inhibitors of gallbladder contraction. Patients treated with somatostatin analogues and those with somatostatinomas have a high incidence of gallstones, presumably due to the inhibition of gallbladder contraction and emptying

CHRONIC CHOLECYTITIS

Recurrent attacks of biliary colic, with only temporary occlusion of the cystic duct, can cause inflammation and scarring of the neck of the gallbladder and cystic duct. This process causes fibrosis as histologic evidence of repeated self-limited episodes of inflammation and is

called chronic cholecystitis. The two types of chronic cholecystitis are chronic calculous cholecystitis and chronic acalculous cholecystitis. However most cases of chronic cholecystitis are commonly associated with cholelithiasis.

AETIO PATHOGENESIS OF GALLSTONES

Gallstones form as a result of solids settling out of solution. The major organic solutes in bile are bilirubin, bile salts, phospho- lipids, and cholesterol. Gallstones are classified by their cholesterol content as either cholesterol stones or pigment stones. Pigment stones can be further classified as either black or brown.

Clinical classification of gallstones

1. Pure cholesterol stone: 10%
2. Pigment Stone: 15%
3. Mixed stone: 75-80%

These can be analysed by colour chromatography, thin layer chromatography and X ray diffraction.[15]

Cholesterol Stones

Pure cholesterol stones are uncommon and account for <10% of all stones. They usually occur as a single large stone with a smooth surface. The majority of cholesterol stones are mixed but are at least 70% cholesterol by weight in addition to variable amounts of bile pigments and calcium. These stones are usually multiple, of variable size, and may be hard and faceted or irregular, multilobed, and soft. Most cholesterol stones (>90%) are radiolucent, though some have a high calcium carbonate component and become radioopaque.

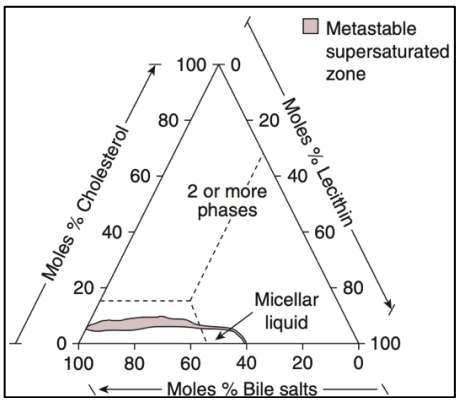


Figure 11: Cholesterol stone formation

The main cause is supersaturation of bile with cholesterol. Cholesterol is highly nonpolar and its solubility in water and bile depends on the relative concentration of cholesterol, bile salts, and lecithin. Cholesterol is secreted into bile and is surrounded by bile salts and phospholipids to form a soluble vesicle complex. When cholesterol hypersecretion is present, increased saturation occurs. When cholesterol concentrations exceed the ability of the bile salts and phospholipid to maintain solubility, the cholesterol precipitates out of solution into a solid, forming a cholesterol stone.

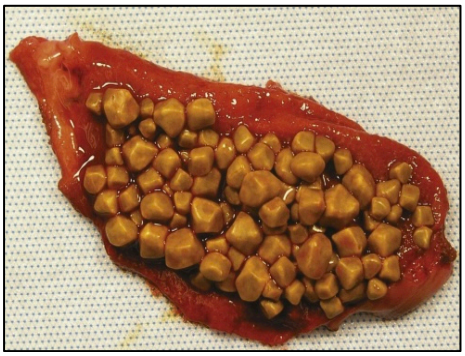


Figure 12: cholesterol stones

Pure pigment stones

They are multiple, small and dark. Pigmented stones contain <20% cholesterol and are dark because of the presence of calcium bilirubinate. Calcium bilirubinate stones found in oriental countries are associated with ascariasis or escherichia coli. Pure pigment stones occurring without any infection but sometimes with haemolysis. These stones are dark or reddish brown and fragile. Some stones are black or dark green.[16] There are two type of pigment stones- black pigment stones and brown pigment stones.

Black pigmented stones are small, dark coloured and spiculated. Formed due to supersaturation of unconjugated bilirubin in the bile. The insoluble unconjugated bilirubin will then precipitate with calcium as insoluble calcium bilirubinate, forming a pigment stone. Normally the process of deconjugation happens at a slow rate. In disorders such as hereditary spherocytosis and sickle cell disease there is increased rate of production of unconjugated bilirubin.

Brown stones are brownish yellow in colour, soft and have a small diameter. Bacteria such as Escherichia coli secrete glucuronidase that enzymatically cleaves conjugated bilirubin to produce the insoluble unconjugated bilirubin. This unconjugated bilirubin then precipitates with calcium, and along with dead bacterial cell bodies, forms soft brown stones in the biliary

tree. Other causes of brown pigment stones are parasitic infections- Ascaris lumbricoides, Clonorchis sinensis.

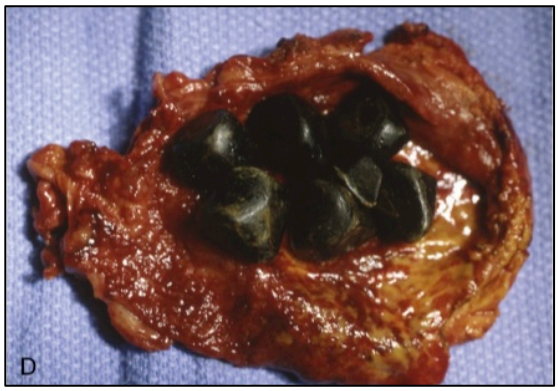


Figure 13: Pigment stones

Mixed Stones

These form the majority of the stones [75-80 %] which are multiple and multifaceted. The central portion of the stones represent the events occurring during initial stages of stone formation. They contain cholesterol, pigments, protein and sometimes parasites.

RISK FACTORS FOR GALL STONE FORMATION

Demography

Oriental countries are more affected than the western world.[17] Indian studies at Aligarh College concluded that mixed stones are the predominant variety in India. Among the Orientals, Japan records the highest prevalence of pigment stones. Rurals are more affected than urban population. This is ascribed to the fact that parasitic infestation of the biliary tract is common in rural Japan. But evidences supporting these are lacking.

In Asians, brown pigment stones are common, and frequently associated with Escherichia coli infected bile. The location of stones also differs from the cholesterol stones.[18] The pigment stones mainly occupy the gall bladder and the common bile duct. Intrahepatic pigment stones are unknown.

Rate appears to be the highest in the Scandinavian countries and Northern Europe while North and South America have higher incidence. Sub-Sahara and Asia reports very low incidence. Puma tribes of Arizona had the highest prevalence around 70 % due to its biological disposition to formation of the gallstones. The prevalence of cholesterol stones is higher in

North-India. Kashmir in particular had the highest prevalence of the cholesterol stones which is comparable to Western Countries.

Age

Like that of cholesterol stones, the frequency of pigment stones increases with age. Predominantly seen during the 5th to 7th decade.[19] Before the 1st decade, pigments stones have been rarely reported in cases of congenital haemolytic diseases. The greatest incidence occurs between the 5th and 8th decade. Incidence is rare below 20 years old. In females gallstones tend to occur more than in males, irrespective of the age, race etc.

Sex

According to various western texts, femaleness is not a risk factor for gall stone. Indian studies show increased incidence in female sex. After puberty the ratio between females to males is 3:1 to 4:1 Females are affected more and possible hypothesis are due to oestrogen and progesterone effects.

Obesity

In untreated obesity, hepatobiliary tract disease is very much prevalent. The liver plays a key role in hyperlipidaemia. Predisposition to the gallstone formation can be attributed to increased biliary cholesterol secretion in concert with changed nucleating factors and altered motility Patient who tries to reduce weight by very low calorie diets, have high risk of the gall stone formation. Obesity has no definite role in the pigment stone formation.[1] Pancreatitis, total paraenteral nutrition and the advanced primary hyperparathyroidism are associated with pigment stones.

A large study conducted in obese people [1006 samples] shows in men and women of the 5th decade with obesity an increased incidence of gallstones -1.7% and 1.8 % respectively. This is not very high when compared with that in the same age group without obesity. In these obese patients, triglycerides were found to be high. Based on these observations, various mechanisms of gall stone formation in obese individuals are postulated.

1. Increased saturation of bile in obese individuals due to excessive biliary secretion of cholesterol.

2. Cholesterol synthesis is related to HMG CO-A reductase enzyme. HMG CO-A reductase production is related to plasma insulin which is higher in obese persons and high fat intake also increases this enzyme.

Haemolytic anaemia

Conditions with decreased life span of red blood cells including haemolysis from prosthetic heart valves, malaria, haemoglobinopathies and membrane defects like hereditary spherocytosis are associated with pigment stones. Probably the increased production of conjugated bilirubin into bile leads to increased formation of stones but evidences are lacking.

Infected bile

This is the oldest theory of gallstone formation. No infection – No stone. The Naunya's theory had got general support. Hence the nidus of stones is formed not only by bacteria, but also by inflammatory exudate or cellular exfoliation, parasites, and ova. Moynihan had aptly described “Gallstone is a tomb stone erected to the memory of organism within it". Bile bathing the gallstones is infected in Japanese.[20]

The most common infecting organism is Escherichia coli, a producer of beta glucuronidase which increases bile saturation by increasing unconjugated water insoluble bilirubin. Addition of glucuronidase, to bile in vitro resulted in the precipitation of calcium bilirubinate. D-glucuronic acid, an inhibitor of glucuronidase prevented the formation of calcium bilirubinate.[26] Mechanisms other than the deconjugation of bilirubin may also be involved in the association of the pigment stones with biliary infection.

Ascaris lumbricoides, round worm eggs are effective nucleating agents for the precipitation of calcium bilirubinate in vitro and may play similar part in vivo. Over half of the stones examined in a large series in Japan showed ova of ascaris lumbricoides. Another report from Vietnam showed this that roundworm eggs were found in 70% of gallstones there. Parasitic infestation causes inflammation of the gall bladder as well as local chemical changes favourable to the precipitation of calcium salts.

Inflammation does the following

1. Reduces the gall bladder motility.
2. Distorts the intrahepatic bile ducts.

3. Interferes with the concentrating capacity of bile within the gall bladder and impairs the cholesterol dissolving capacity of the bile in gall bladder.[13]

Effects of estrogen and progesterone

Estrogen

Several studies have confirmed that an association between gall stone and use of exogenous estrogens, whether as oral contraceptives, post-menopausal oestrogen replacement.

The possible mechanisms are explained as follows

1. Decreased chenodeoxycholic acid
2. Increased cholesterol saturation
3. Increased cholesterol secretion
4. Cholestasis occurring with oestrogens

A definitely higher prevalence of gall stones among the females are documented in many studies throughout the world. This sex difference appears to be being around the age of puberty and disappears around menopause. Like oral contraceptives, endogenous oestrogen also reduces bile acid pool and increases cholesterol secretion and the saturation thereby increasing gall stone formation. Multiparity also shows an increased incidence of gall stones.

Progesterone

The effect of progesteron are as follow's:

- Saturates bile
- Relaxes smooth muscle which in-turn impair gall bladder emptying.

Family history

Only first degree relatives have two fold risk while others studied showed no relationship. Siblings have a higher incidence of gall stone disease.[22]

Parity

With increasing parity, the gall stones are more common in young women probably due to repeated attacks on gall bladder by altered physiology of oestrogen or progesterone on the biliary composition and smooth muscle function of the biliary apparatus.[23]

Diet

High calorie diet

Increased incidence of gallstones in persons taking high calorie diet was noted in France.[Sarles,1968]. This relation was obtained when matched for sex, body weight and the level of physical activity. The results suggested that adiposity and high caloric food increased cholesterol secretion which predisposed them for gall stone formations. High consumption of simple sugars predisposes individuals to gall stone formation. An inverse relation to serum cholesterol had been reported.[24]

Low calorie diet

Concern had been expressed that weight reduction diets might favour the formation of lithogenic bile through a marked reduction in bile acid secretion. This increase in lithogenic bile occurs through a marked reduction in bile acid secretion. Possible events that lead to formation of the gallstones in patients who were dieting for weight reduction is shown in the flow chart

High cholesterol diets

The exogenous cholesterol can contributes to the biliary cholesterol pool and increases its saturation. The main problem in man is that the cholesterol is not converted to bile acid unlike in animal species ;instead it is re-excreted many times by the liver . The magnitude of increase is modest, however suggesting that the effects of excess dietary cholesterol on bile composition are not as great as those associated with increased cholesterol synthesis.

Poly unsaturated fatty acid [PUFA]

There were conflicting reports regarding the increased incidence of gall stones associated with intake of food rich in PUFA chronically for years.

Fiber

Lack of dietary vegetable fibre had been suggested as a possible cause of a variety of gall bladder diseases. However, there are no reliable data to this point. Studies of diet rich fibre versus low demonstrate a reduction in the cholesterol saturation of bile in pigment stones. But a recent study executed carefully, proved no relation between them.[25]

Alcohol

Modest level of alcohol 30-60 milligrams per day reduces the risk. Alcohol causes increase in high density lipoprotein and reduction in low density lipoprotein, by which the biliary cholesterol saturation is reduced. Pigment stones are more common among patients with cirrhosis as compared. The mechanism underlying this association is unknown, although the hypersplenism and mild haemolytic anaemia that often accompany cirrhosis might be suspected of contributing to this increased incidence of gallstones.

Diabetes

A study regarding diabetes and the gallstones reported that the incidence of the gallstones in diabetics is 30 %. There is progressive increase in the incidence of the gallstones occurring in each age group beyond the third decade in both female and male diabetics, white and coloured. In diabetics beyond 50yrs of age, the gallstones were present in approximately one out of every two white women.

Increased risk of gallstone formation associated with diabetes is attributed [26] to

1. Supersaturation of bile with Cholesterol.
2. Fatty infiltration of the liver with altered lipid metabolism.[32]
3. Hyperinsulinemia and its effects on lipids
4. Gallbladder dyskinesia due to autonomic neuropathy.

Drugs

Effects of Cholesterol lowering drugs Clofibrate

An increased frequency of the gallstones among users of clofibrate had been shown in two large clinical trials of the efficacy of this drug in heart diseases. The specific mode of its action on lipids is not known but there is a definite increase in the incidence of gallstones. These findings are suggestive of increased mobilisation of cholesterol from body fat stores by clofibrate which predisposes them for stone formation.

An increased incidence of gallstones among users of bile acid sequestrants had not been documented. When used alone they have no effect on cholesterol and bile acid metabolism. They act by trapping bile acids in the gut and , increasing their faecal loss, thereby decreasing the total bile acid pool. But compensatory increase in cholic acid in liver prevents excessive

loss of bile acids. When these drugs are combined the loss of bile acid is marked with increased lithogenicity.

Oral Contraceptives

Its role is described in detail with effects of estrogen [exogenous] on gallstone formation. There is a definite increased incidence of gall stones among contraceptive pill users.[33]

Effects of gastro intestinal disorders and surgeries

Ileal disease, resection and bypass

Bile acids are absorbed throughout the length of the intestine, but especially in the ileum, where transport is more active. Bile acids return via portal vein and are re-secreted into the bile in combination with newly synthesised bile acids. Bile acid synthesising capacity of liver is compromised in most of the patients due to disease process itself, which limits the normal functions of liver.

Truncal Vagotomy

The gall bladder and the biliary tract are supplied by celiac plexus, which loses its connections due to vagotomy. It may alter the physiology of the gall bladder emptying, leading to stasis. It may lead to formation of the gallstones. This was long debated matter. But there is no definite increase in the incidence of the gallstones following truncal vagotomy as pointed out by various studies because the gall bladder becomes adapted to the situation in a matter of 3 months till then irregular emptying was noted.

Cystic fibrosis with pancreatic insufficiency

An increased prevalence of the gallstones had been noted among children with cystic fibrosis.[34] The possible mechanism ascribed are

1. Increased mucus production and abnormal mucus, leads to nucleation of stones
2. Interference with bile flow → stasis → promotes gallstone growth[30]
3. Reduced bile acid pool due to interference of bile acid re-absorption due to poorly secreating pancreas.

PATHOLOGY

Chronic calculus cholecystitis occurs to repeated bouts of mild to severe acute cholecystitis. Super saturation of bile predisposes to both chronic inflammation and, stone formation. In chronic calculus cholecystitis the complete obstruction of bile flow does not occur. Since most gallbladders that are removed at elective surgery for gallstones show features of chronic cholecystitis, one must conclude that biliary symptoms often emerge following long-term coexistence of gall- stones and low-grade inflammation.

The morphologic changes in chronic cholecystitis minimal. The serosa is usually smooth and glistening but may be dulled by sub serosal fibrosis. Dense fibrous adhesions may remain as sequelae of pre-existent acute inflammation. On sectioning, the wall is variably thickened, and has an opaque grey-white appearance. In the uncomplicated case the lumen contains green-yellow, mucoid bile and usually stones. The mucosa itself is generally preserved. On histologic examination the degree of inflammation is variable. In the mild cases, only scattered lymphocytes, plasma cells and macrophages are found in the mucosa and in the subserosal fibrous tissue.

In more severe cases there is marked subepithelial and subserosal fibrosis, accompanied by mononuclear cell infiltration. Reactive proliferation of the mucosa and fusion of the mucosal folds may give rise to buried crypts of epithelium within the gallbladder wall. Outpouchings of the mucosal epithelium through the wall (Rokitansky- Aschoff sinuses) may be quite prominent. Presence of acute inflammatory changes implies acute exacerbation of an already chronically injured gallbladder.

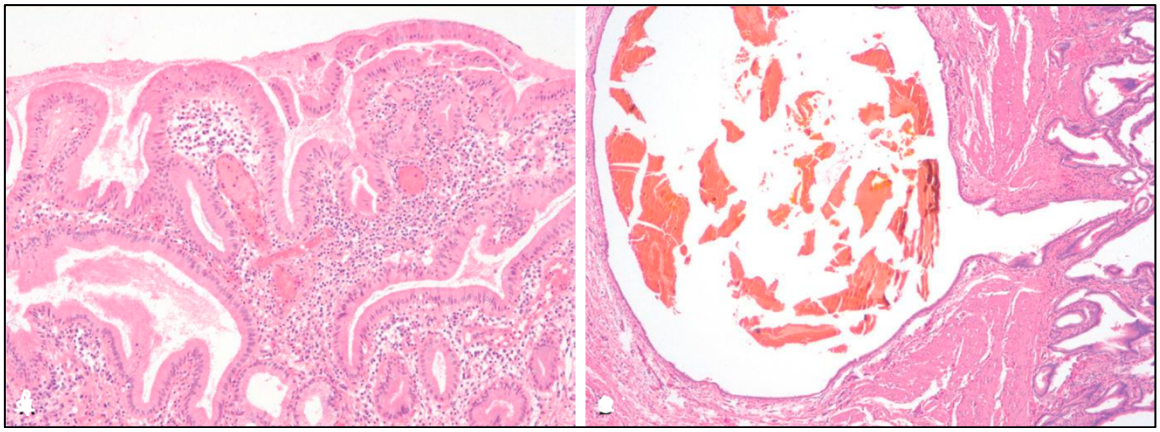


Figure 14:Histological appearance of chronic cholecystitis with Rokitansky- Aschoff sinuses

CLINICAL FEATURES

The most common presentation feature of chronic calculus cholecystitis, is right upper quadrant pain. The pain may develop after taking a heavy fatty meal, known as dyspepsia. The nature of pain is dull and constant. The other presentation symptoms are flatulence, intolerance to fatty food. Biliary colic pain is seen in 10-20% of the patients.

On examination most of the patients are normal. Some patients have right hypochondrial pain. Most of the time the symptom is non-specific. The differential diagnosis such as peptic ulcer disease, chronic pancreatitis, should be considered.

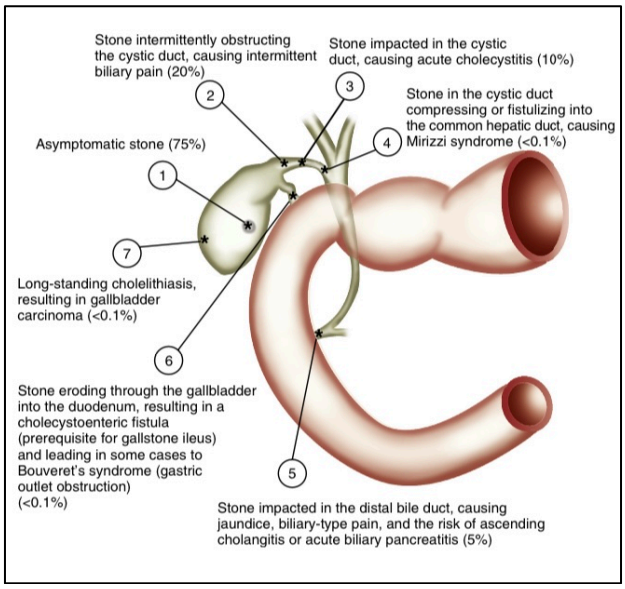

Stone intermittently obstructing the cystic duct, causing intermittent biliary pain (20%)
Stone impacted in the cystic duct, causing acute cholecystitis (10%)
Stone in the cystic duct compressing or fistulizing into the common hepatic duct, causing Mirizzi syndrome (<0.1%)
Asymptomatic stone (75%)
Long-standing cholelithiasis, resulting in gallbladder carcinoma (<0.1%)
Stone eroding through the gallbladder into the duodenum, resulting in a cholecystoenteric fistula (prerequisite for gallstone ileus) and leading in some cases to Bouveret's syndrome (gastric outlet obstruction) (<0.1%)
Stone impacted in the distal bile duct, causing jaundice, biliary-type pain, and the risk of ascending cholangitis or acute biliary pancreatitis (5%)
1
2
3
4
5
6
7

Figure 15:Description of the pathology

INVESTIGATIONS

Diagnosis of chronic calculus cholecystitis is made mostly based on radiological findings. The laboratory investigations do not show any abnormality in most of the cases.

Plain abdominal radiographs

The films are usually obtained in AP projection. Special view to visualise the gall bladder like penetrated AP film over the gall bladder area in a suspected case of calculous Cholecystitis is more contributory to the surgeon. The gall bladder lies usually parallel to spine at the level of 11th and 12th ribs.[31] Fundus lies usually in opposition to the duodenal cap and anterior to renal shadow. Only 10% of the gallstones are radio opaque, in contrary to renal

stones, which are 90% radio opaque. 10 -20% of cholesterol stones and 50% of pigment stones are radio opaque. The opacity is due to the presence of calcium greater than 4% as carbonate or phosphate. Rarely calcification of the gall bladder wall and presence of air when communication exist between the intestine and the gall bladder as fistula can be detected.

Figure 16:X-ray showing radio opaque stones

Oral cholecystography [OCG]

Until mid 1970's oral cholecystogram was the golden standard for the evaluation of the gall bladder diseases. With the advent of ultrasonogram and hepatobiliary scintigraphy the role of cholecystogram has become very much limited, almost virtually eliminated from routine investigations of cholelithiasis and biliary tract pathologies. Graham and Cole introduced oral cholecystography Iopanoic acid [T elepaque] and Sodium tyropaonate [Bilipaque] are the dyes commonly used. Standard dose is 3g [6 tablets of telepaque].Patient is advised to avoid fat for 3 days. At 9 pm tablets are taken orally. Overnight fast is observed. X -rays are taken on next day morning at 9 am. A fatty meal is given and X-ray is taken after 45 minutes. This film will show contractability of the gall bladder. If the gall bladder is not visualized a double dose [6g] is given and re-examined.

If the gall bladder still not visualized, the gall bladder disease is certain. Visualisation of the gall bladder depend on both cystic duct patency and the gall bladder mucosal capacity to absorb water and concentrate the contrast. Presence of filling defects that seeks gravitational dependency are diagnostic of cholelithiasis. Floating stones indicate high cholesterol content. Contrast material adheres to the surface of the stone and mimics calcified rim [salzmann effect].

Filling defect not moving when patients position is altered is unlikely to be a gallstone. The accuracy of oral cholecystogram is around 90%.

Ultrasonogram

In imaging the gall bladder, ultrasonogram is a primary diagnostic technique. The revolution brought about by ultrasonogram is attributed to its simplicity, repeatability and non-invasiveness. Rapid diagnosis of the gall bladder disease is done and bilary tract pathology is diagnosed without a need of exposure to ionising radiation, medication, double dose examination.

The surgeon feels more secure and definite when operating on a patient with cholelithiasis shown by USG than with a non-visualised gall bladder of oral cholecystography. Static or real time grey scale B mode equipment with transducers, frequencies ranging between 2.5 to 5.0 MHz are used. 5 MHz frequency allows best resolution "and assessment of the size. Focal zone is the narrowest part of the beam that must be matched to the location of stone for best image. Fasting for 6-8 hrs prior to examination is required.

Major Criteria for cholelithiasis are

1. Echogenic focus
2. Acoustic shadow
3. Gravitational dependence.

The specificity is 90 %, sensitivity is 85 %, accuracy is 95 % and false negativity is 2-9 %. In 10-15% cases gallstones may be missed mostly when they are less than 5mm in size, especially when impacted at the neck of the gall bladder. Sometimes in very obese and fatty individuals USG had some difficulties. The normal size of the common bile ductis4-7mm.

Figure 17:USG showing cholelithiasis

CT Scan

This is not a routine investigation. But useful in very fatty persons when USG fails to give a clear picture. No special preparation is needed other than fasting for 12 hrs. A series of 8-10 transverse and 5-6 longitudinal scans are performed. It is also useful in patients with a large amount of gas in the bowel and in jaundice when an associated cause can be eliminated precisely. Its sensitivity could never equal that of an ultrasonogram. Also exposure to radiation is always there.

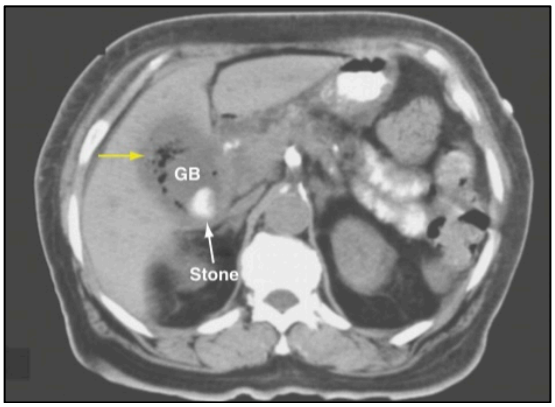


Figure 18: CT scan showing cholelithiasis

Intravenous cholangiogram

With the advent of modern and safe, non invasive diagnostic modalities the role of intravenous cholangiogram had almost become a history rather than a rare investigation, which was once upon a time was a routine investigation of the biliary tract diseases. After 1970 with the advent of P T C, ERCP, USG and C T Scan, nowadays cholangiogram is rarely done.

The contrast material used is methyl glutamine Ioglycamate [cholegraffin or Biligraffin] 20 ml dose 52 % solution. It is given intravenously as infusion. It appears in bile in few minutes and permits the radiological visualisation of the bile passages than the gall bladder. Oral cholecystography is superior in visualising the gall bladder.

Indications[32]

- Intolerability to oral contrast materials.
- Post Cholecystectomy syndromes.

Contraindications

- Raised plasma bilirubin < 3 mgm/100 ml.
- Impaired Renal and liver functions
- Previous 0 C G within 48 hours.
- Paraproteinemia's
- Thyrotoxicosis
- Sensitivity to contrast materials.

Following could be assessed in IV Cholangiogram

- Duct size, termination, filling defects in the lumen
- Flow of contrast into the duodenum
- Any retrograde filling of the intrahepatic radicles.

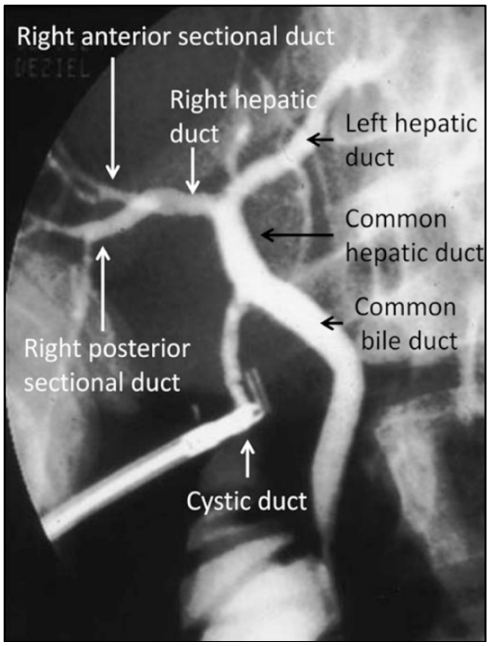


Figure 19: Intravenous cholangiogram

Percutaneous transhepatic cholangiography:

Huard and Doxylon Hop first described the technique of percutaneous transhepatic cholangiography in 1937. The procedure was sparingly used for 30 years due to lack of fine chiba needles [23 gauge]. Till the introduction of Chiba needles 18 gauge needles were used which resulted in high incidence of intraperitoneal haemorrhage and laparotomy subsequently.

Technique

A duct which should be within the liver to lessen the chance of intraperitoneal bile leakage is chosen. Fluoroscopy or image intensifier is ideal both for introduction of the needle and during the injection of the dye. After preparation and draping, needle is introduced in the 8th or 9th intercostal space in the midaxillary line parallel to the table. Failure to enter the biliary tree is common particularly if the ducts are not dilated. Virtually all dilated ducts are opacified during the procedure.

Indications

- Obstruction in Biliary tract.
- To know the site of obstruction.
- Failure of ultrasonogram and C T Scan in showing dilated ducts in a case of obstructive jaundice case.

Contra Indications and Preventive measures

- Significant coagulopathy from any cause
- Significant Ascites
- History of allergy to contrast material
- Suspected right lobe liver abscess
- Suspected case of Hydatid cyst.

Complications

- Sepsis [most common]- 3%
- Biliary Leak - 1-2%
- Haemorrhage - 2%
- Death - 0-0.9%

Interpretation

In a normal study both common bile ducts, right and left hepatic ducts are visualised. The cystic duct and the gall bladder may not be visualised.[33] But it doesn't imply cystic duct obstruction always. But in a distal CBD obstruction absence of the gall bladder indicates cystic duct obstruction or cholecystectomy. The site of obstruction will be delineated clearly but cause may not be predicted always. Filling defects in the lumen indicates gallstones.

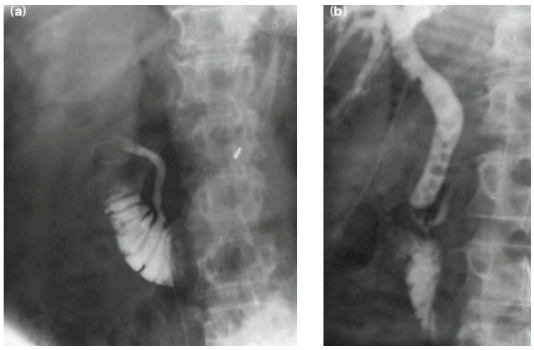


Figure 20: Percutaneous transhepatic cholangiogram

Endoscopic retrograde cholangiopancreatography [ERCP]

In 1972 Kasugai et.al, first reported a success rate of 97 % in using fibroscopes to cannulate the ampulla of Vater. With the advent of side viewing endoscopy, today the success rate is almost 100 % in cannulating ampulla of Vater and injecting contrast dyes to visualise the biliary tract and the pancreatic system. ERCP is far superior to C T Scan and ultrasonogram study, because it gives an accurate delineation of the anatomy of the biliary and pancreatic ducts. Bile duct is cannulated if the cannula tip is directed to wards 11 or 12 0' clock position approaching from below. If cannulation is difficult a precutaneous sphincterotomy is useful. The contrast. Injection into the ductal system should be done under fluoroscopy to avoid over injection there by preventing pancreatitis. A normal cholangiogram shows biliary system with a smooth outline of the CBD normal CBD measures within 7 to 10 mm. Filling defects indicates gallstones.

Indications

- In post-cholecystectomy symptoms to demonstrate any dilatation of C B D due to stones.
- In case of obstructive jaundice to know the level of obstruction.[34]
- As a pre-therapeutic procedure before removing CBD stones

Interpretation

Radiographically gallstones can be detected as filling defects in the ducts.

Limitations

ERCP is a complex procedure requires an experienced endoscopist, fluoroscopy control and side viewing duodenoscopes. The facilities are mostly lacking in smaller hospitals. So PTC

seems superior to ERCP in our country.[35] Cost of ERCP is also high. ERCP may be used primarily to evaluate biliary and pancreatic disease in the absence of jaundice, after cholecystectomy and when percutaneous transhepatic cholangiography is contraindicated or failed.

Figure 21: ERCP showing calculi

Magnetic retrograde cholangio pancreatogram [MRCP]

MRCP is a magnetic resonance imaging, which is used to detect biliary duct pathologies. It is highly sensitive in detection of biliary duct obstruction. No contrast is required during the study.

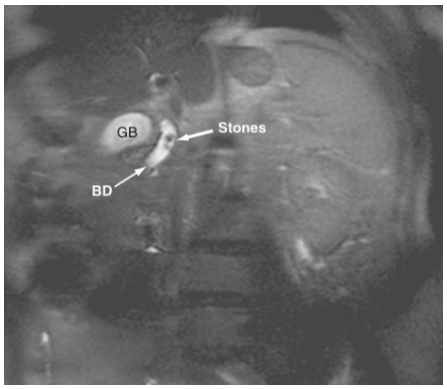


Figure 22: MRCP showing calculi

Radioisotope scans

A Rose Bengal and 99 m Tc labelled derivatives of iminodiacetic acid dimethyl [HIDA], Diethyl ID A or Isopropyl [DI5ID A] are used. Usual dose is 5 mg. 80 % of the isotope is excreted in bile and 20 % in the urine. It allows visualisation of the biliary tree even in hyperbilirubinemia up to 20 m g m/100mI. This detects acute cholecystitis almost in all cases. The role of radio isotope scans are very much limited in the diagnosis of cholelithiasis. So this is not indicated in chronic calculous cholecystitis.

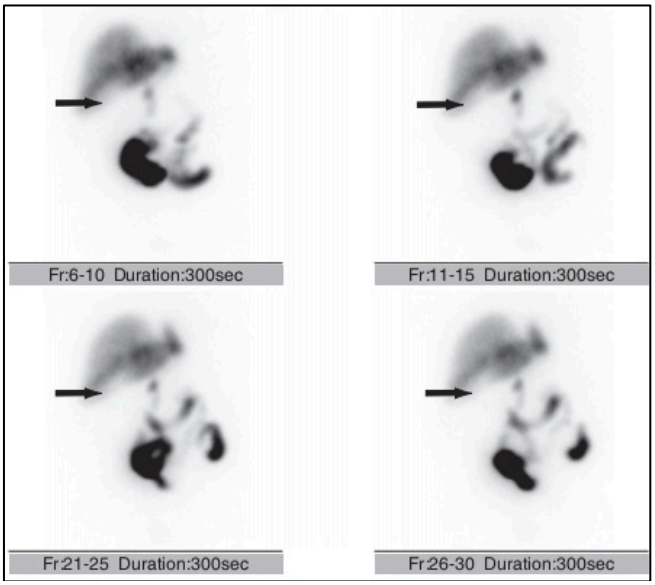


Figure 23: HIDA scan

MANAGEMENT

Gall stone dissolution

Oral dissolution therapy

Thistle & Schoenfield et.al, [were the first to show that oral administration of chenodeoxycholic acid to women with gallstones produced a significant rise in the ratio of Cholesterol solubilising agents to cholesterol in bile. These results were confirmed by Bell, Whitney and Dowling et.al. [36]

Dose and duration

Chenodeoxycholic acid in a dose of 5-25 mgm /kg of body weight had been tried in various trials, but 15 mgm/kg of body weight is adequate. Duration of the treatment varies between 6 months and 2yrs depending on the size of the gallstones. Periodical ultrasonogram is needed to confirm that stones are dissolving.

Ursodeoxycholic acid, another agent to cause definite dissolution of gall bladder gallstones had equal efficacy with lesser diarrhoea and hepatotoxicity.

Side effects:

1. Diarrhoea due to secretion of water and electrolytes by the colonic mucosa.
2. Hepatotoxicity.

3. Promotion of atherosclerosis.
4. Risk of carcinoma gall bladder & colon.

Limitataions:

Success rate is only about 40% . If the treatment is discontinued the chance of increase in the size is almost 100% . Even after complete dissolution the recurrence rate is very high.[37] Oral dissolution is unsuitable for our tropical setup for the following reasons [Nundy and Tandon, 1988].

1. Expensive and unavailable.
2. Considerable drop out of patients
3. Poor patient compliance
4. Tendency to induce calcification of gallstone during the. treatment.
5. Cholesterol stones are rare in our country.

Percutaneous cholecystolithotomy:

Recently Kellet and others [1988] have reported that gall stones can be removed from otherwise normal functioning gall bladders. It may prove to be complimentary to dissolution therapy or shock wave lithotripsy. This is performed with patient under G. A. adopting method and instruments used for one stage percutaneous nephrolithotomy. Potential complications such as bile leakage are likely to limit the use of this procedure.[38]

Shock wave for gallstones:

Brendel and Enders[1983] from Germany have used shock wave treatments to treat kidney stones in humans. This same group have used similar shock waves for successful treatment of gallstones in humans. Just over four fifths of the 200 treated patients had a solitary stone less than 30 mm in diameter, and the remainder had two or three smaller stones. Adjuvant treatment with a combination of chenodeoxycholic and ursodeoxycholc acids was given to dissolve stone fragments. Shock waves were guided by ultrasound. Patients were immersed in water and given either epidural or intravenous analgesia. Stones were fragmented in all but two patients. Side effects included mild pancreatitis in two patients and transient haematuria in 3 percent. Only patients with a radiologically functioning and contracting gall bladder are suitable for this therapy. This technology is expensive and will not yet be available in most countries.

Dissolution and flushing of bile duct stones:

Flushing may be done with saline, heparinized saline or lignocaine Saline, via the T tube with pressure less than 30 cm H20 to prevent cholangio-venous reflux and septicemia. The relaxation of sphincter of oddi may be acquired with synthetic peptide ceruletide. Dissolution may be tried with Cholate infusions but its efficacy is very 1ow . So Mono-octanoin which more actively clears the stones is widely used. But the most effective agent is methylterbutylether [MTBE] which ,is capable of achieving gallstone dissolution within hours of instillation, in pure cholesterol stones.

SURGICAL MODALITIES:

Cholecystectomy is the ideal surgery for symptomatic calculous cholecystitis(44). It may be either early or interval. It had got another dimension recently whether open or laparoscopic. Early cholecystectomy in a carefully prepared patient in younger age groups had death and morbidity similar to elective cholecystectomy done 6-8 weeks after an acute attack. Surgical treatment can be done either laparoscopically (laparoscopic cholecystectomy) or open cholecystectomy.

Open cholecystectomy:

A right paramedian or right subcostal incision is made.[40] Soon after the abdomen is opened the whole biliary and pancreatic areas and the liver are examined for congestion, friability, any signs of ascending cholangitis or stones in the bile ducts.

All steps of the operation must be carried out under direct vision with careful packing. A large abdominal pack is used to push away the colon and a Deaver's retractor pulls this down and to the left, so that the upper margin of the duodenum is exposed. A second pack with Deaver's retractor pushes the stomach to the left and slightly up wards. A long rectangular type of retractor is placed medial to the gall bladder close to under surface of the liver in order to rotate the liver slightly upward and thus a better view of porta hepatis is obtained. Division of the visceral peritoneum: The peritoneum over the free edge of gastro-hepatic omentum is incised for 2-3 cms near the area of the cystic duct and the porta hepatis and pushed side wards so that the cystic artery, cystic duct and bile ducts are exposed well.

Cholecystectomy starting at the cystic duct. This is the more generally accepted procedure. By securing cystic artery first, three things are accomplished:

- The subsequent dissection is carried out in a relatively dry field;
- After the division of cystic artery, the cystic duct uncoils itself and will be straightened out and clearly defined up to the common bile duct.
- It eliminates the danger of serious bleeding from tearing of the cystic artery through traction upon the gall bladder. Since the cystic artery is a fine vessel, it is better if it is divided using an aneurysm needle. This artery is closely related to the cystic lymph gland of Lundh, which may help in identification of it.

Cholecystectomy starting at the fundus (fundus first approach):

This method is adopted in conditions where the identification of the duct system is more difficult. Such difficulty will arise in acute or chornic cholecystitis. Espiner [1982] had described a modification is indicated when the gall bladder is very much thickened and inflamed, where separation of the gall bladder bed is carried out in the sub mucosal plane using a diathermy.

Laparoscopic cholecystectomy:

It had become popular in just 5 years after its introduction by Mauret [1987]. The principle advantages are short hospital stay and early return to normal activity.[74]

Requirements:

High flow CO2 insufflator, a xenon light source, a cable to convey the high monitor video camera, irrigation devices, electrocautery and laparoscopy and laparoscopic instruments.

Technique:

Under general anaesthesia or epidural anaesthesia pneumoperitoneum is established with the patient in Trendelenberg position. Supra umbilical, epigastric, right mid clavicular and midaxillary 3-5 c m s incisions are made. Cholecystectomy is performed and the gall bladder is delivered through one of the port usually the epigastric. Clips are used instead of ligation since it is simple and easy to apply them.[75]

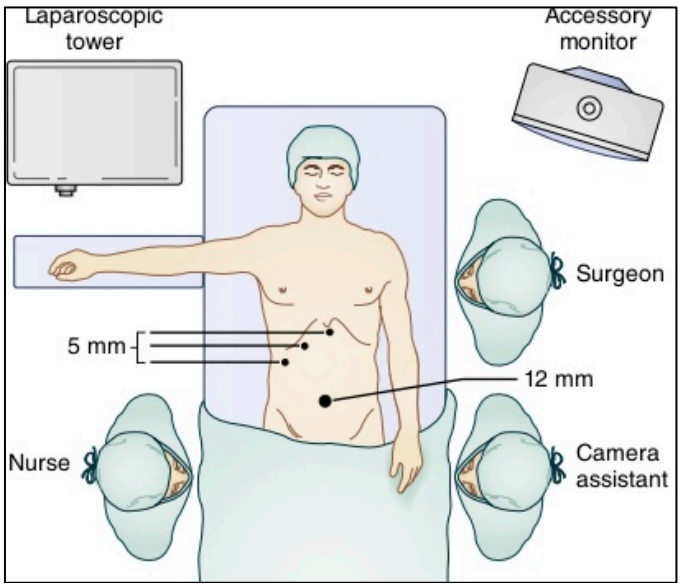


Figure 24: Laparoscopic cholecystectomy port placement

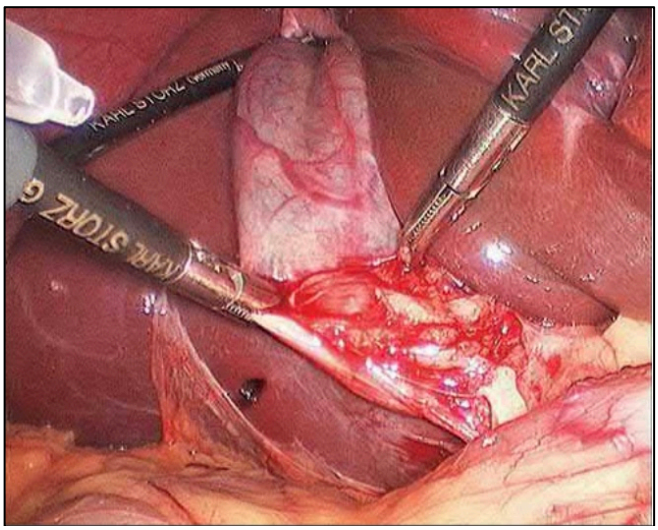


Figure 25: Retraction of gall bladder

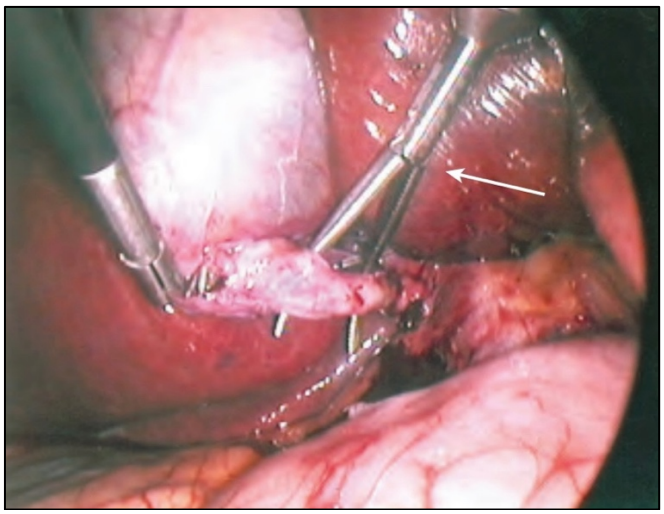


Figure 26: Dissection of the calot's triangle

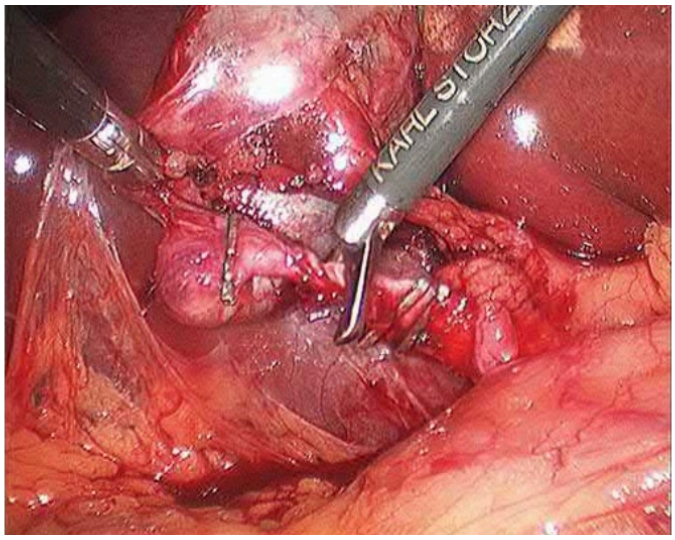


Figure 27: Clipping of the cystic duct

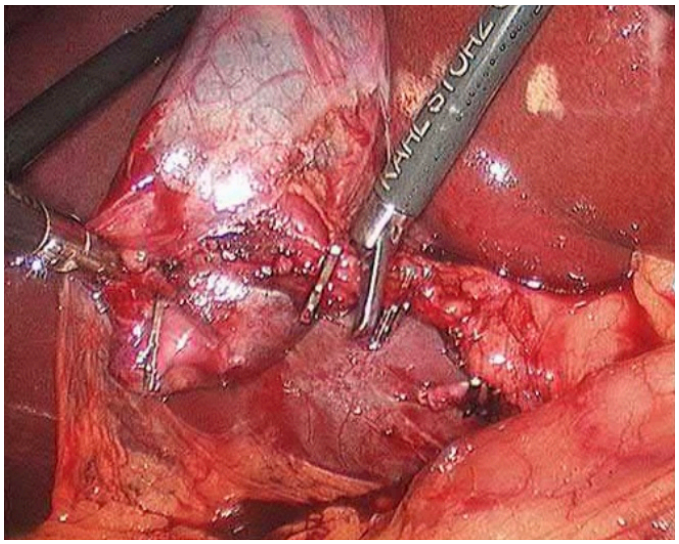


Figure 28: Clipping of the cystic artery

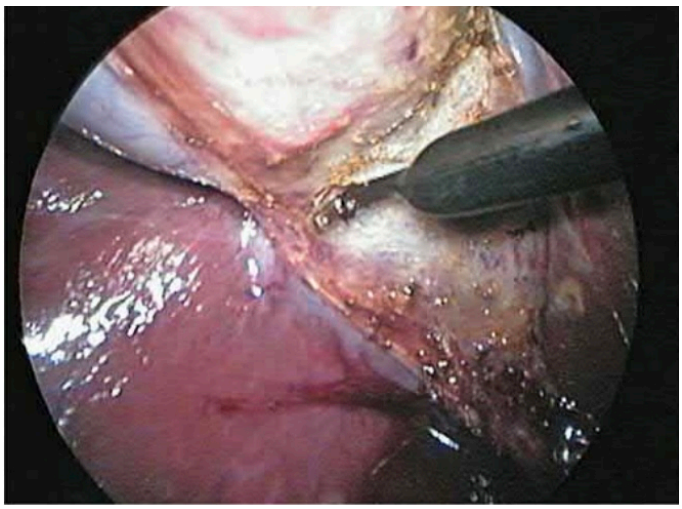


Figure 29: Dissection of the gall bladder from the gall bladder fossa

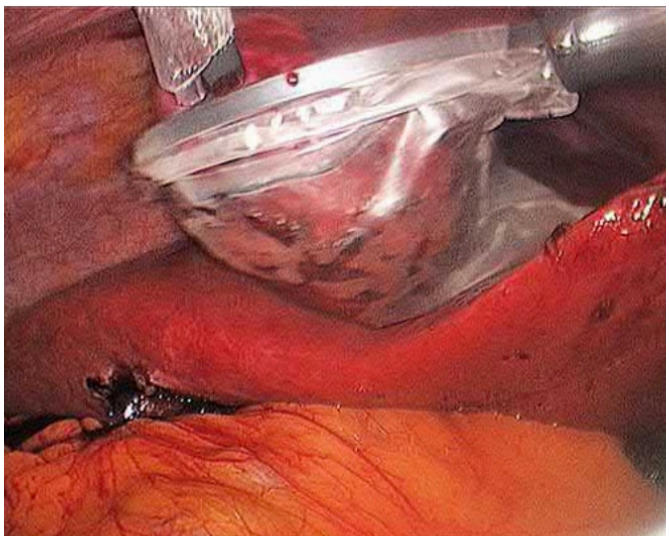


Figure 30: Gall bladder placed in entrapment bag post dissection

Indications:

1. Cholelithiasis and biliary colic
2. Chronic calculous cholecystitis.
3. Symptomatic gall bladder polyps.
4. Resolved gallstone pancreatitis.

In a recent paper by Stahlschmdt M in Oct'92 which compared 816 conventional and 812 laparoscopic cholecystectomies.[Largest series reported at present]. In the conventionally operated group reoperation was required in 2.7% while in laparoscopic procedure it was less than 1.2 %. Death for open procedure is .5 % but for laparoscopic surgery none out of 812 cases. Growing experience and better definition of the contra indications for the laparoscopic cholecystectomy might improve the results in future.

MATERIALS AND METHODS

MATERIALS AND METHODS

Place of study: Department of General Surgery, Santosh Medical College and Hospital, Ghaziabad.

Duration of study: July 2021 to June 2022

Study Design: Prospective observational study

Sample size –

n = Z21-α/2 P(1-P)/l2 = 97 patients

Where, Z= 1.96 at 5% level of significance

P= Prevalence of 50% (from reference article) l = Relative error (20% of P)

Study technique – Convenient Sampling

Study Setting:

The study was carried out among adult patients (18 to 75 years) being referred to Department of Surgery, Santosh Medical College and Hospital, Ghaziabad (Uttar Pradesh) presenting with a H/O Cholelithiasis.

Study Population:

A total of 100 adult patients (18 to 75 years) were recruited in the study. In the present research, presenting complaint of upper abdominal pain was considered for admission. Patients with a diagnosis of chronic calculus cholecystitis were then recruited into the study.

SELECTION OF CASES

Inclusion Criteria:

1. Males and females between age of 18 to 75 years, reporting to Santosh Medical College and Hospital, Ghaziabad (Uttar Pradesh) with c/o upper abdominal pain, h/o cholelithiasis, diagnosed as chronic calculus cholecystitis.
2. Patients agreeing with signed and informed consent.

Exclusion Criteria:

Cases with the following findings were excluded:

1. All patients below 18 years and above 75 years
2. Terminally ill patients
3. Major bleeding disorder
4. Pregnancy
5. Malignancy

Methodology:

After taking the required consent, patients will be assessed under the following parameters:

Preoperative parameter: Laboratory investigation, Radiological investigation

Intra operative parameter: Gross morphology of the gall bladder

Post-operative parameter: Histopathological changes Study tools:

1. History - age, sex, diet, socio-economic status, presenting complaints
2. Clinical examination
3. Investigations:
   Laboratory- CBC, LFT, KFT, Urine R/M
   Radiological- USG whole abdomen
4. Type of surgery- Open or laparoscopic cholecystectomy
5. Gross morphology
6. Histopathological changes

Data management and Statistical Analysis:

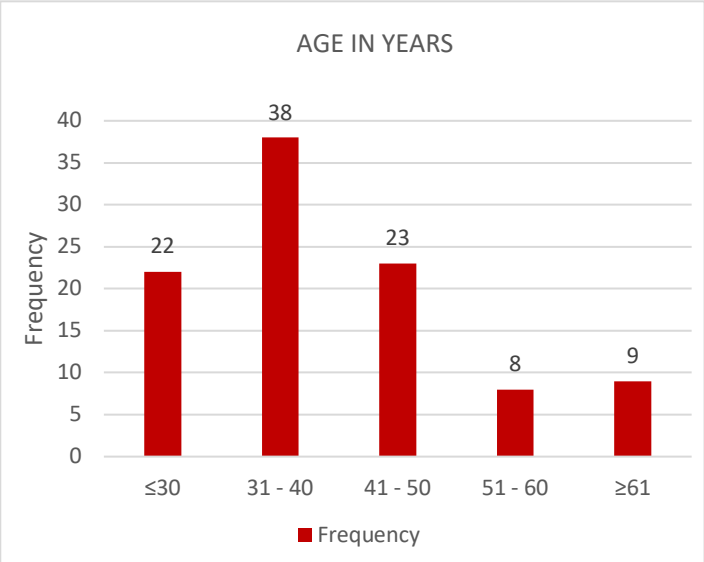
Statistical analysis will be performed using SPSS (Statistical Package for the Social Sciences) for Windows (Trial version). Categorical variables will be described as frequency (percentage), mean ± standard deviation will be used for continuous parameters. For non-parametric variables, the data are presented as median (min-max). In this case, the nonparametric Mann–Whitney test will be used for statistical comparisons. Categorical variables will be compared between two or more groups using the Chi-square test. For all analyses, a two- tailed p-value of <0.05 was considered statistically significant.

RESULTS AND ANALYSIS

RESULT & ANALYSIS

Table 1:Distribution of age in years

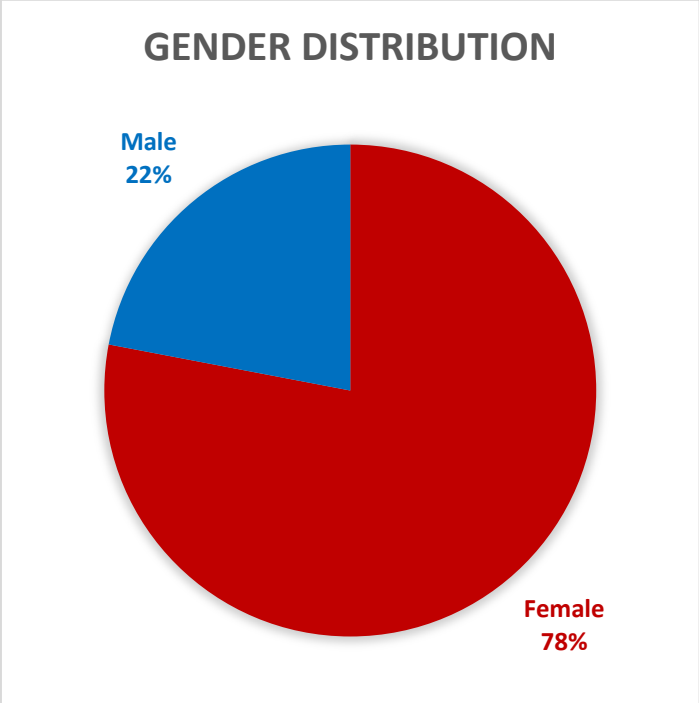
Age In Years	Frequency	Percent
≤30	22	22.0%
31 - 40	38	38.0%
41 - 50	23	23.0%
51 - 60	8	8.0%
≥61	9	9.0%
Total	100	100.0%



Out of the 100 patients included in the study, 22 patients where found to be in 21 – 30 years age group. 38 patients found in 31-40 years age group. 23 patients found in 41-50 years age group. 8 patients found in 51-60 years age group. 9 patients found in 61-70 years age group. One sample Kolmogorov- Smirnov test was done and the value of p is 0.04.

Table 2: Gender distribution

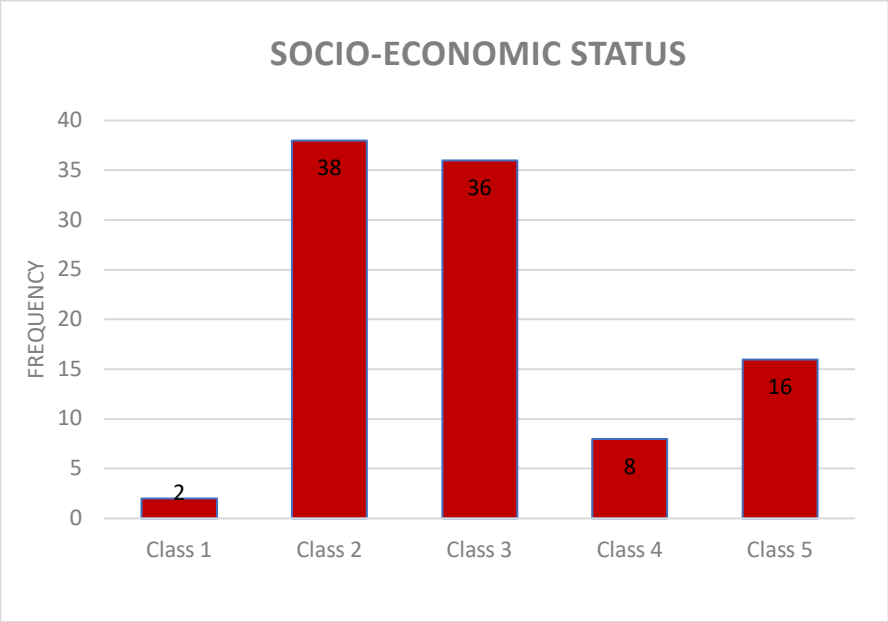
Sex	Frequency	Percentage
Female	78	78.0%
Male	22	22.0%
Total	100	100.0%



Out of the total sample size, 78 where found to be female and 22 where found to be males. 78% of the total sample size where found to be females. One sample binomial test was done and the value of P is <0.001.

Table 3:Distribution of Socio-Economic Status

Socio-Economic Status	Frequency	Percent
Class I	2	2.0%
Class II	38	38.0%
Class III	36	36.0%
Class IV	8	8.0%
Class V	16	16.0%
Total	100	100.0%



In this study, the socio-economic status of the patient was graded according to modified – kuppuswamy's classification. 2 patients(2%) are of class I(upper class). 38 patients (38%)are of class II (upper-middle class). 36 patients (36%) are of class III(lower-middle class). 9 patients(9%) are of class IV(upper-lower class) and 16 patients(16%) are of class V(lower class). One sample chi-square test was done and value of P is <0.001.

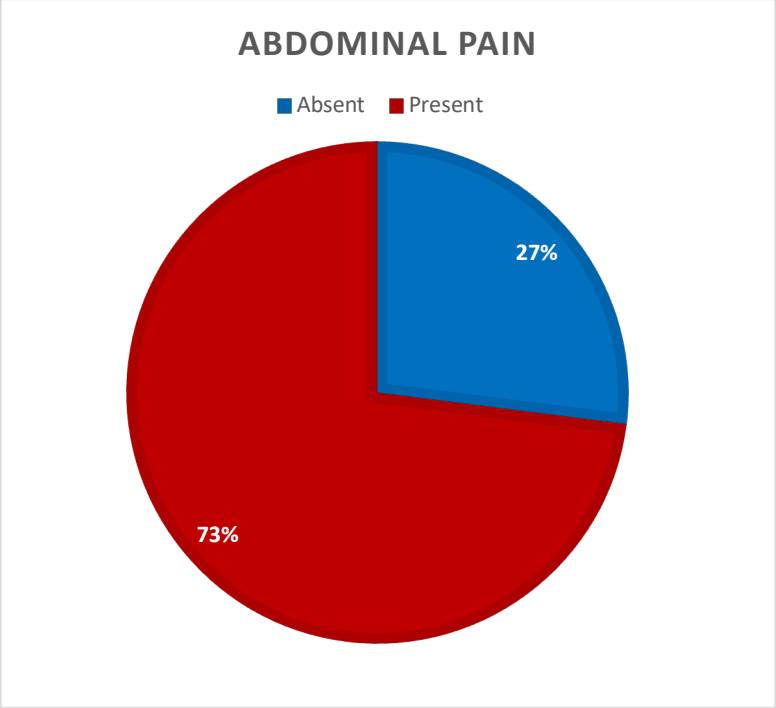
Table 4: Diet

Diet	Frequency	Percent
Mixed diet(MD)	86	86.0%
Vegetarian diet(V)	14	14.0%
Total	100	100.0%

In this study, out of the 100 patients, around 86 patients where found to consume mixed diet and 14 patients where found to consume vegetarian diet. One sample binomial test was done and value of P is <0.001

Table 5:Abdominal pain

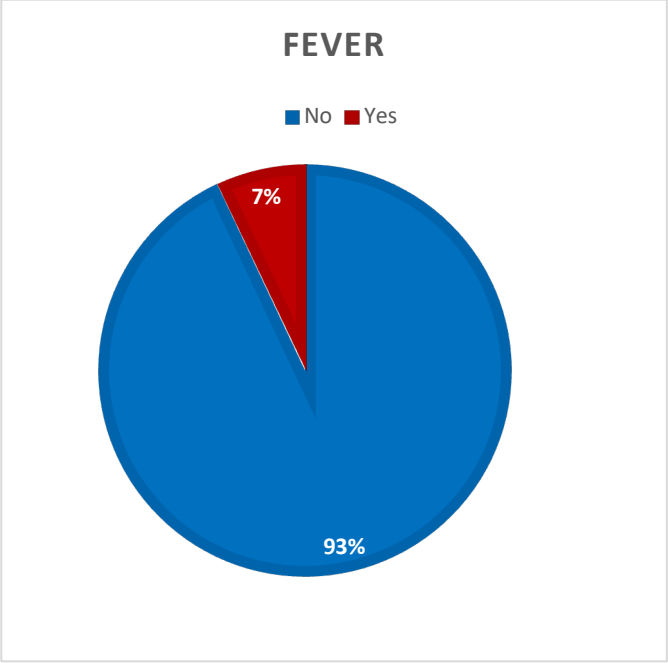
Abdominal Pain	Frequency	Percent
Absent	27	27.0%
Present	73	73.0%
Total	100	100.0%



Out of the total sample size, abdominal pain was present in 73 patients (73%) and absent in 27 patients. (27%). One sample binomial test was done and P value is <0.001

Table 6:Fever

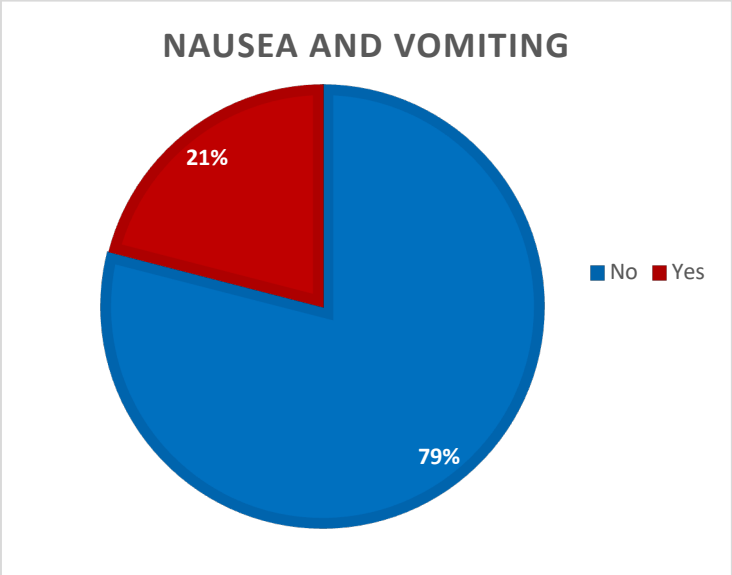
Fever	Frequency	Percent
Absent	93	93.0%
Present	7	7.0%
Total	100	100.0%



Of the 100 patients present, fever was observed only in 7 patients (7%) and absent in 93 (93%) patients. One sample binomial test was done and the P value is <0.001

Table 7:Nausea and Vomiting

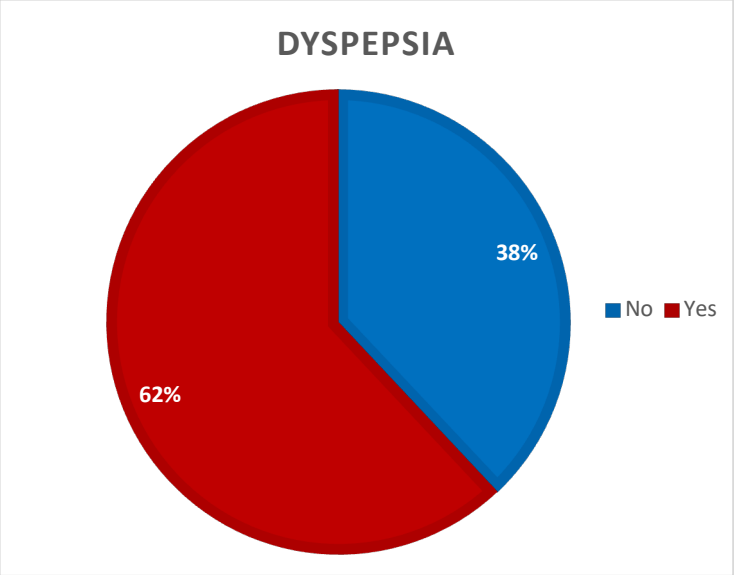
Nausea & Vomiting	Frequency	Percent
Absent	79	79.0%
Present	21	21.0%
Total	100	100.0%



Nausea and vomiting was found in 21 patients (21%) and absent in 79 patients (79%) out of the 100 patients included in the study. One sample binomial test was done and the value of P is <0.001

Table 8:Dyspepsia

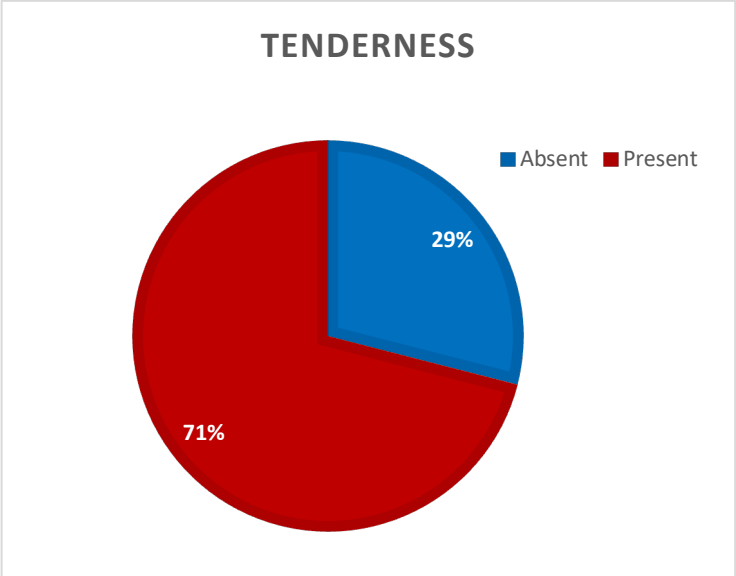
Dyspepsia	Frequency	Percent
No	38	38.0%
Yes	62	62.0%
Total	100	100.0%



Dyspepsia was present in 62 patients (62%) and absent in 38 patients (38%) out of the 100 patients included in the study. One sample binomial test was done and the value of P is 0.021

Table 9: Abdominal tenderness

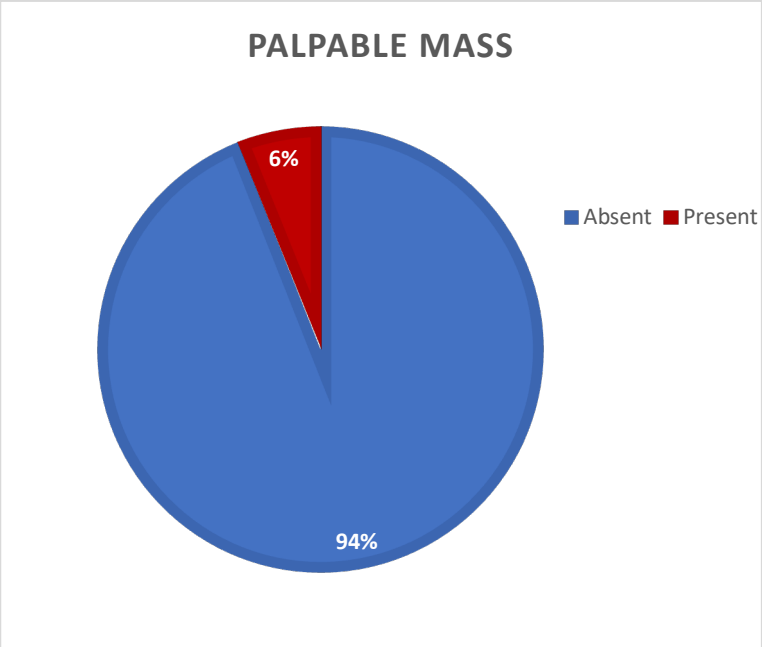
Tenderness	Frequency	Percent
Absent	29	29.0%
Present	71	71.0%
Total	100	100.0%



Abdominal tenderness was present in 71 patients (71%) and absent in 29 patients (29%) of the 100 patients present in the study. One sample binomial test was done and the value of P is <0.001

Table 10: Palpable mass

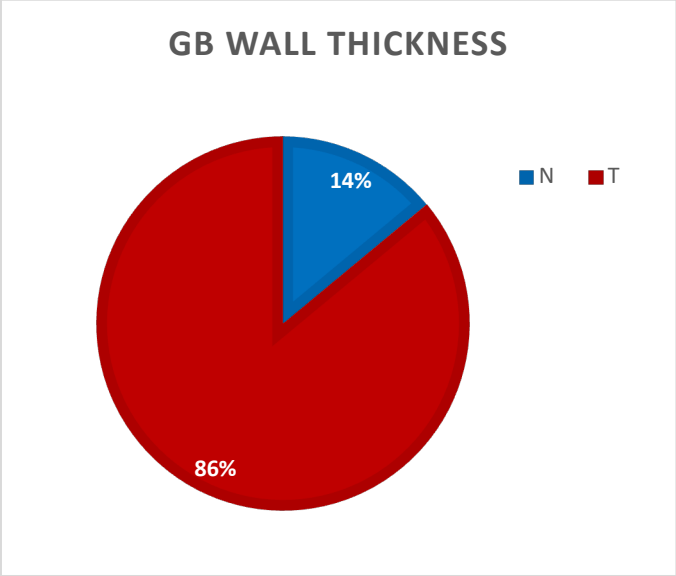
Palpabale Mass	Frequency	Percent
Absent	94	94.0%
Present	6	6.0%
Total	100	100.0%



Palpable mass was present only in 9 patients (9%) and absent in 94 patients (94%) of the 100 patients in the study. One sample binomial test was done and the value of P is <0.001

Table 11: Gall bladder wall thickness in USG

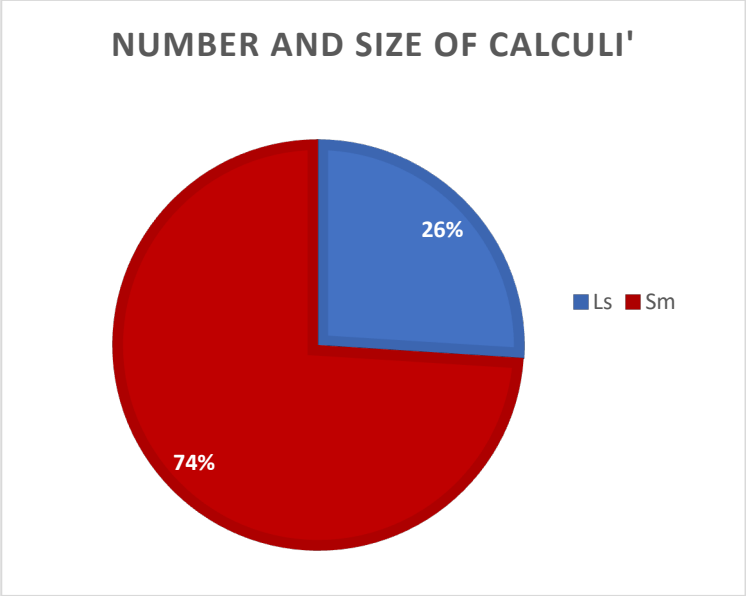
Gb Wall Thickness	Frequency	Percent
Normal thickness(N)	14	14.0%
Thick(T)	86	86.0%
Total	100	100.0%



Ultrasound showed that gall bladder wall thickness was observed in 86 patients (86%). Gall bladder wall was found to be normal in 14 patients (14%). One sample binomial test was done and the value of P is <0.001.

Table 12:Number And Size Of Calculi in USG

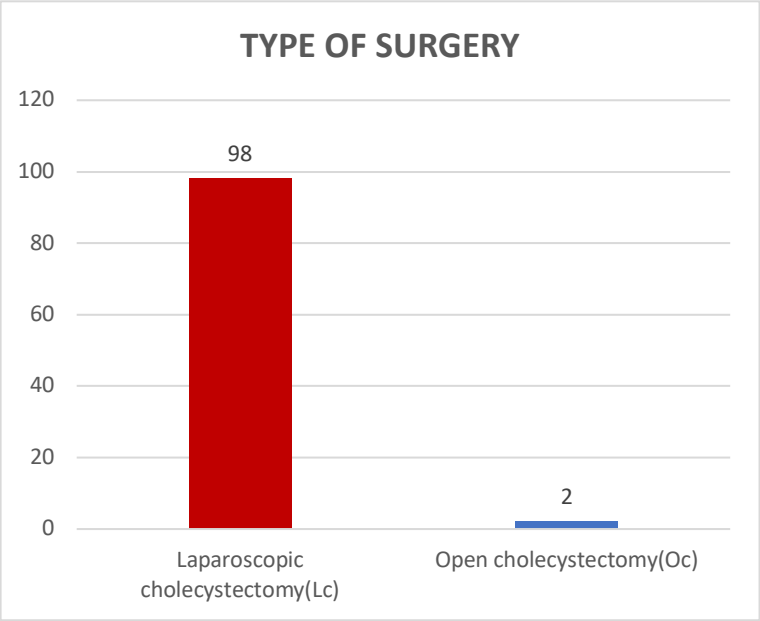
Number And Size Of Calculi	Frequency	Percent
Large single calculi(Ls)	26	26.0%
Small multiple calculi(Sm)	74	74.0%
Total	100	100.0%



Ultrasound showed that 74 patients had small and multiple calculi (74%). 26 patients (26%) had large and single calculi. One sample binomial test was done and the value of P is <0.001

Table 13:Type Of Surgery

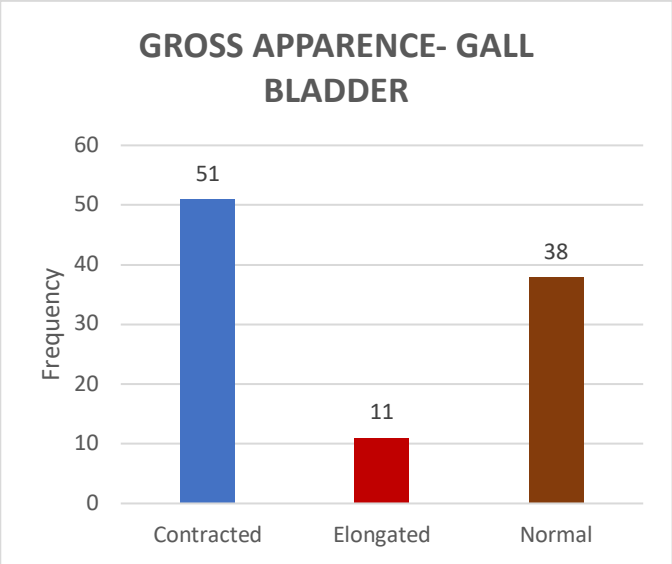
Type Of Surgery	Frequency	Percent
Laparoscopic cholecystectomy(Lc)	98	98.0%
Open cholecystectomy(Oc)	2	2.0%
Total	100	100.0%



Out of the 100 patients, 98 patients underwent laparoscopic cholecystectomy and 2 patients underwent open cholecystectomy. One sample binomial test was done and the value of P is <0.001.

Table 14: Gross appearance of gall bladder

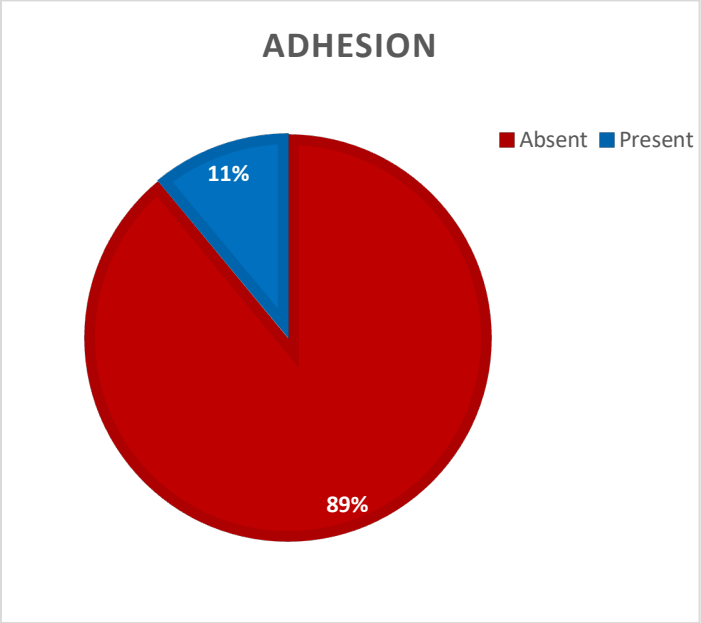
Gall Bladder Gross	Frequency	Percent
Contracted	51	51.0%
Elongated	11	11.0%
Normal	38	38.0%
Total	100	100.0%



Intra-operatively the gross appearance of gall bladder was observed. Gall bladder was contracted in 51 patients (51%). Gall bladder grossly was found to be elongated in 11 patients (11%). Gall bladder was grossly found to be normal in 38 patients (38%). One sample chi-square test was done and value of P is <0.001.

Table 15: Adhesions

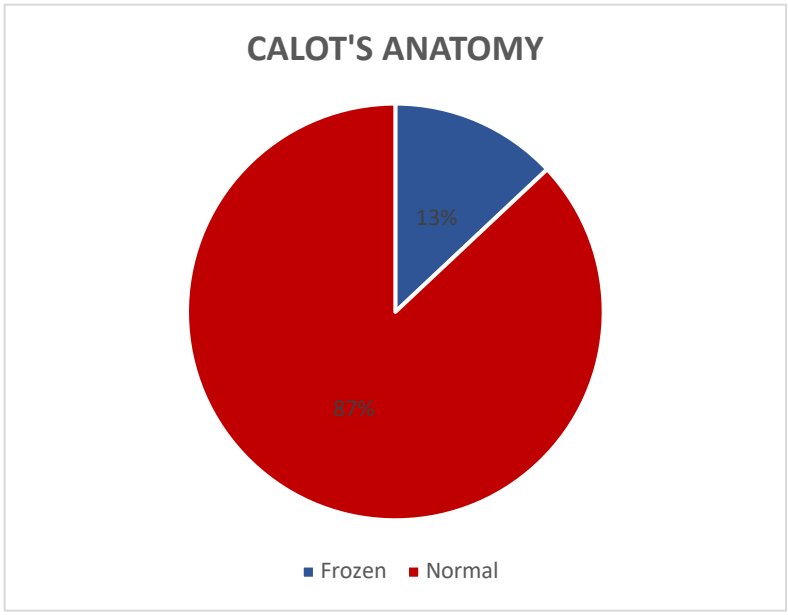
Adhesion	Frequency	Percent
No	89	89.0%
Yes	11	11.0%
Total	100	100.0%



While doing laparoscopic/open cholecystectomy, intraoperatively adhesion's where looked for and observed that in 89 patients adhesion where absent(89%) and in 11 patients adhesions where present.(11%). One sample binomial test was done and P was found <0.001.

Table 16: Calot's anatomy

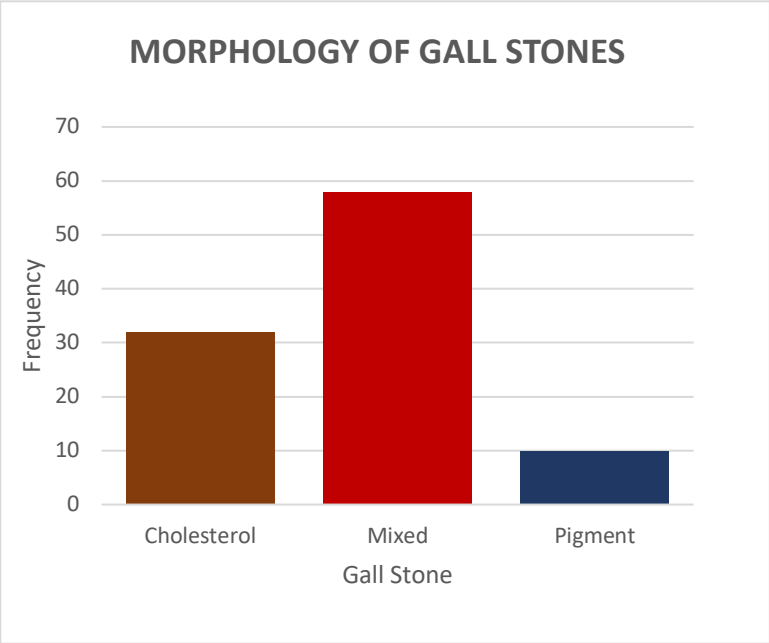
Calot's Anatomy	Frequency	Percent
Frozen	13	13.0%
Normal	87	87.0%
Total	100	100.0%



Intra-operatively calot's anatomy was observed and in 89 patients (89%) calot's anatomy was observed to be normal and in 13 patients (13%) calot's anatomy was found to be fibrosed. One sample binomial test was done and p value is <0.001.

Table 17:Morphology of gall stones

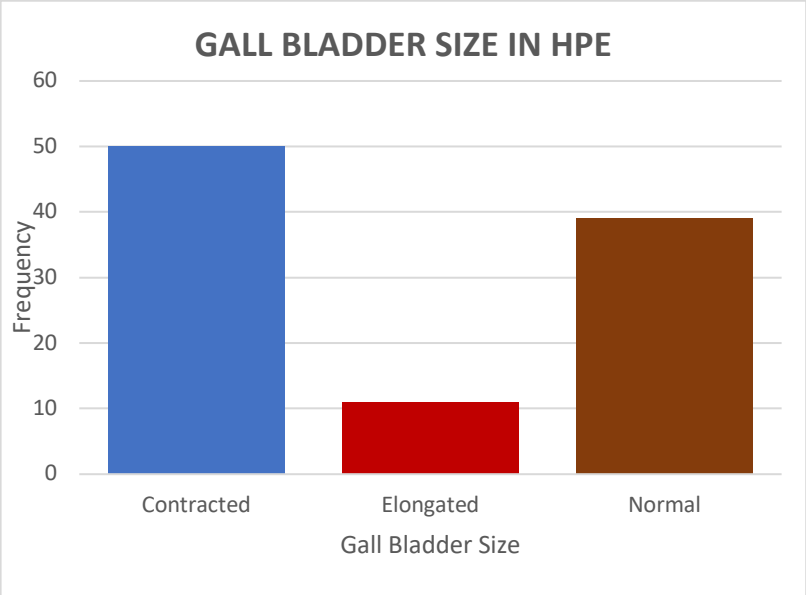
Gall Stone	Frequency	Percent
Cholesterol	32	32.0%
Mixed	58	58.0%
Pigment	10	10.0%
Total	100	100.0%



Intraoperatively, 32 patients (32%) have cholesterol stones. 58 patients (58%) have mixed stones and 10 patients (10%) have pigmented stones. One sample chi-square test was performed and p value is <0.001.

Table 18:Gall Bladder Size in HPE

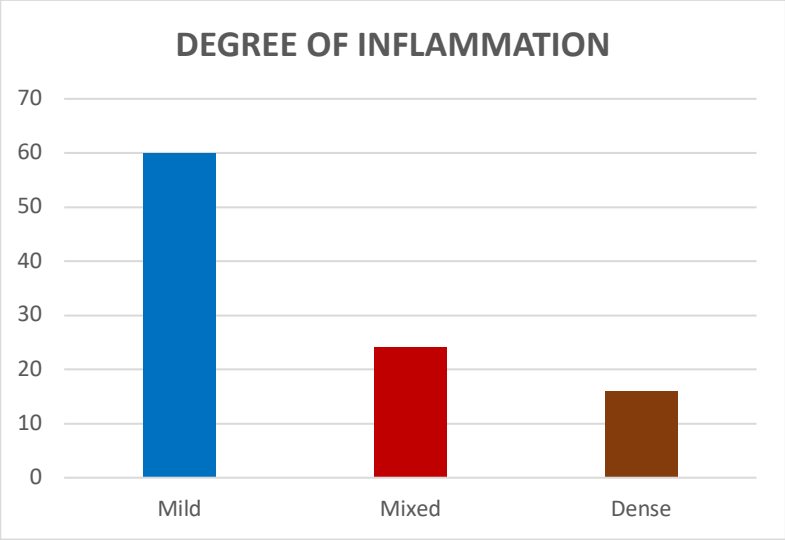
Gall Bladder Size	Frequency	Percent
Contracted	50	50.0%
Elongated	11	11.0%
Normal	39	39.0%
Total	100	100.0%



During histopathological examination, 50 patients (50%) where found to have contracted gall bladder. 11 patients (11%) where found to have elongated gall bladder and 39 patients (39%) where found to have normal gall bladder. One sample chi-square test was performed and p value was <0.001.

Table 19:Degree Of Inflammation

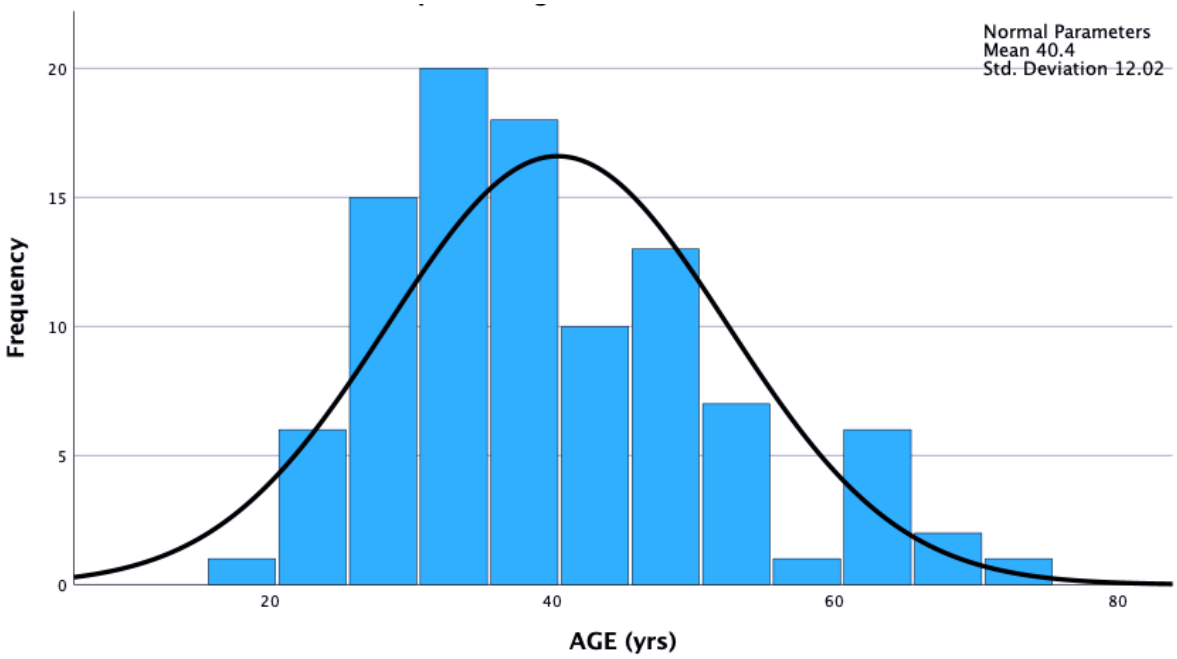
Degree Of Inflammation	Frequency	Percent
Mild	60	60.0%
Mixed	24	24.0%
Dense	16	16.0%
Total	100	100.0%



Histo-pathologically, the gall bladder specimens where examined. According to the degree of inflammation they where graded. 16 patients (16%) have dense inflammation. 24 patients (24%) have mixed inflammation and 60 patients (60%) have mild inflammation. One sample chi-square test was done and P value is <0.001.

Table 20:Distribution of mean Age (Yrs)

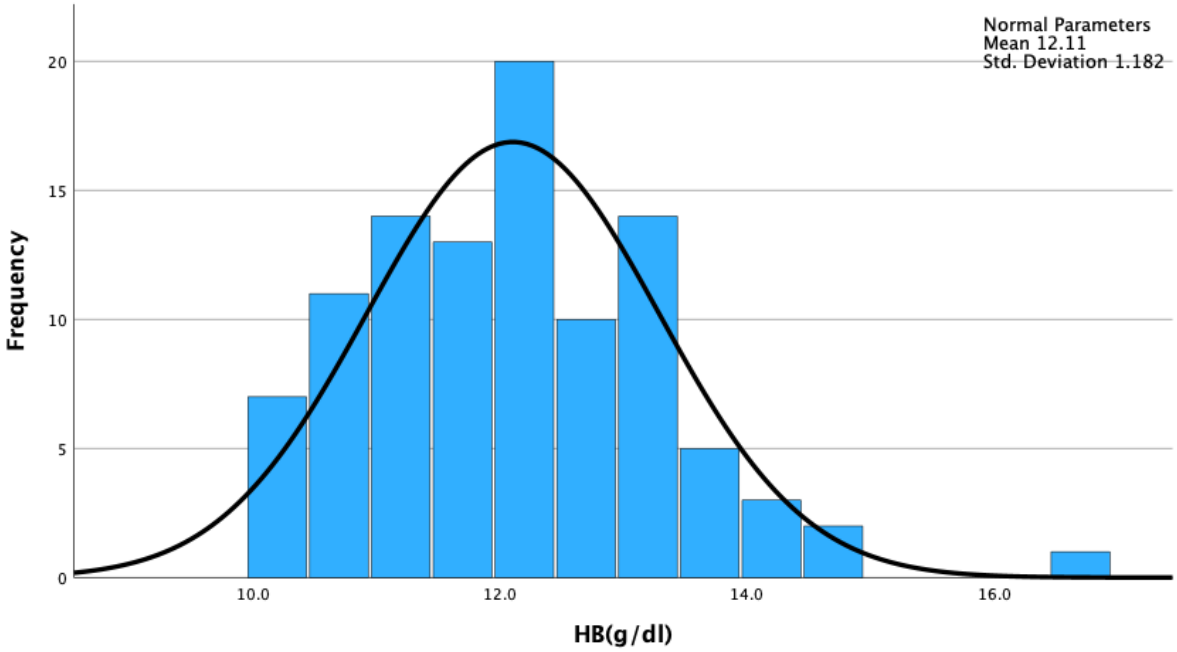
	Number	Mean	SD	Minimum	Maximum	Median
Age (Yrs)	100	40.3600	12.0181	18.0000	73.0000	40.0000



The age group of all the 100 patients in the study where analysed, and the mean age was found to be 40.4 and standard deviation is 12.08. The minimum age was found to be 18yrs and the maximum was found to be 73yrs.The value of p after one-sample Kolmogorov-Smirnov Normal Test is 0.004.

Table 21:mean HB (g/dl)

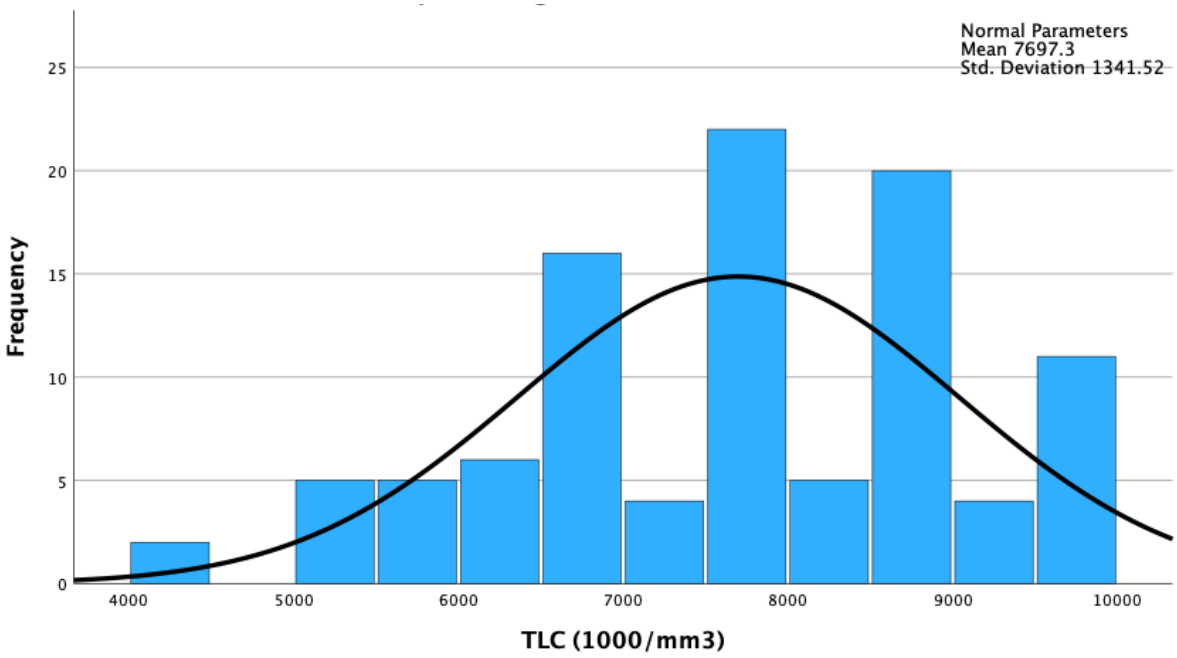
	Number	Mean	SD	Minimum	Maximum	Median
HB (g/dl	100	12.1070	1.1820	10.2000	16.9000	12.1000



The haemoglobin levels of all the 100 patients in the study where analysed, and the mean age was found to be 12.11 and standard deviation is 1.18 The minimum haemoglobin was found to be 10.2mg/dl and the maximum was found to be 16.9mg/dl .The value of p after one-sample Kolmogorov-Smirnov Normal Test is 0.2.

Table 22:mean TLC (1000/mm3)

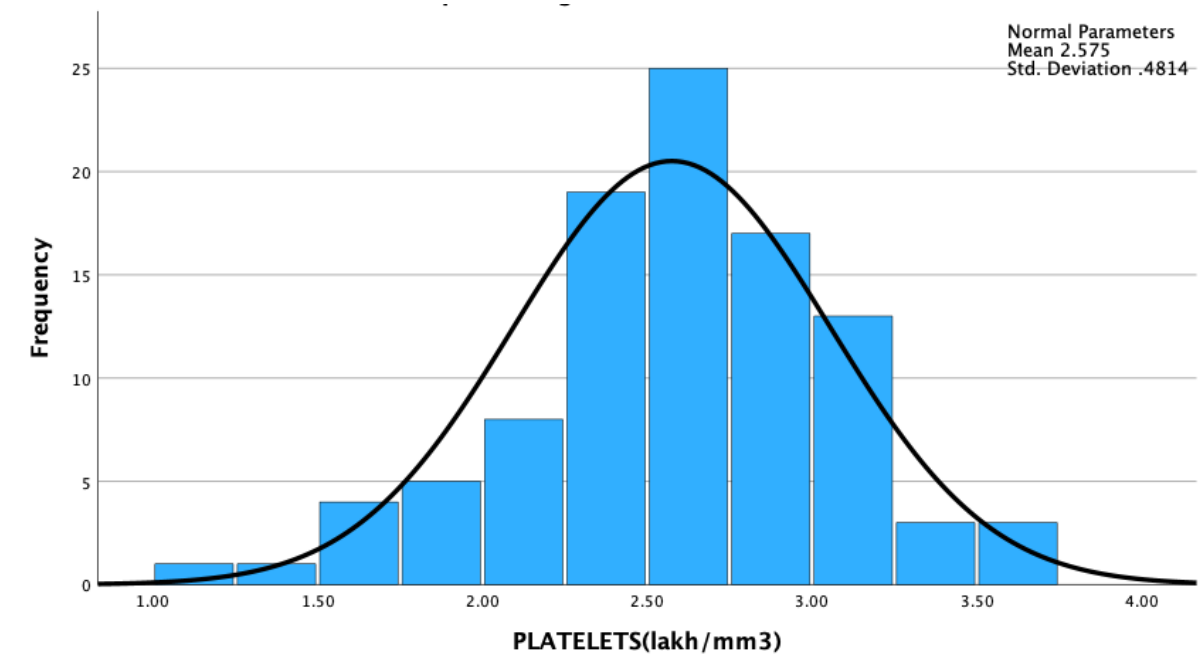
	Number	Mean	SD	Minimum	Maximum	Median
TLC (1000/mm3)	100	7697.3100	1341.5195	4395.0000	9872.0000	7689.0000



The total leucocyte count(TLC) levels of all the 100 patients in the study where analysed, and the mean TLC was found to be 7697.3 and standard deviation is 1341.52 The minimum TLC was found to be 4395 and the maximum was found to be 9872 .The value of p after one-sample Kolmogorov-Smirnov Normal Test is 0.005

Table 23: mean Platelets (lakh/mm3)

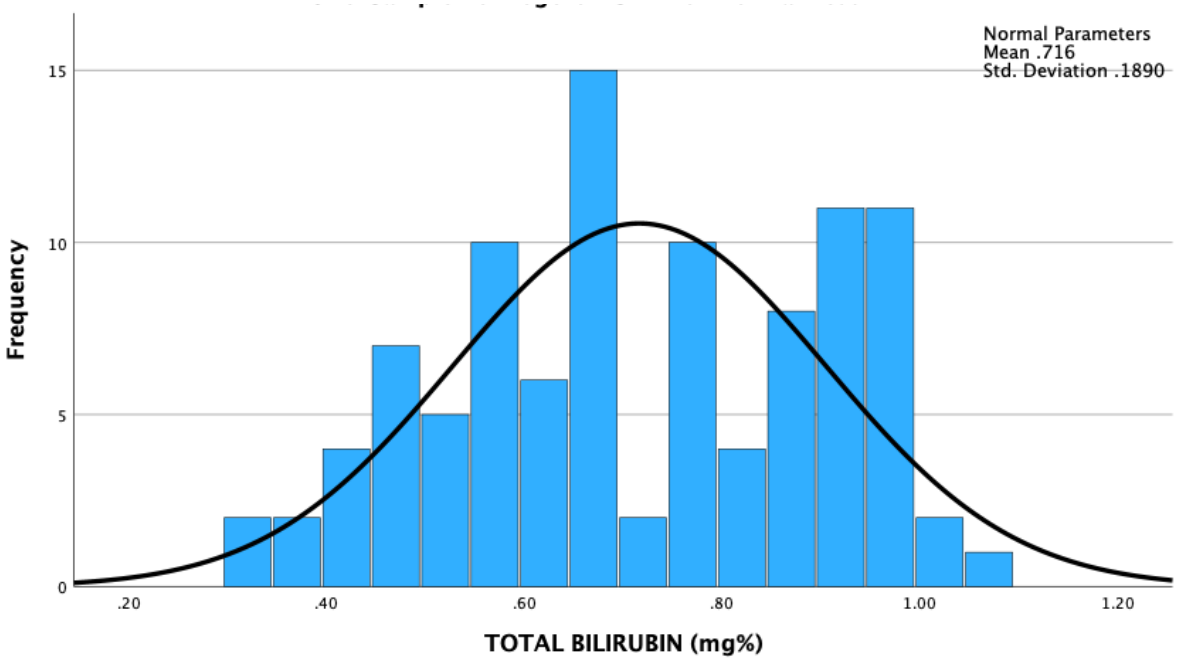
	Number	Mean	SD	Minimum	Maximum	Median
Platelets (lakh/mm3)	99	2.5747	.4814	1.1400	3.7200	2.5000



The platelet levels of all the 100 patients in the study where analysed, and the mean platelet count was found to be 2.5 lakh/mm^3 and standard deviation is 0.48. The minimum platelet count was found to be 1.14 lakh/mm^3 and the maximum was found to be 3.7 lakh/mm^3 .The value of p after one-sample Kolmogorov-Smirnov Normal Test is 0.026

Table 24:mean Total Bilirubin (mg%)

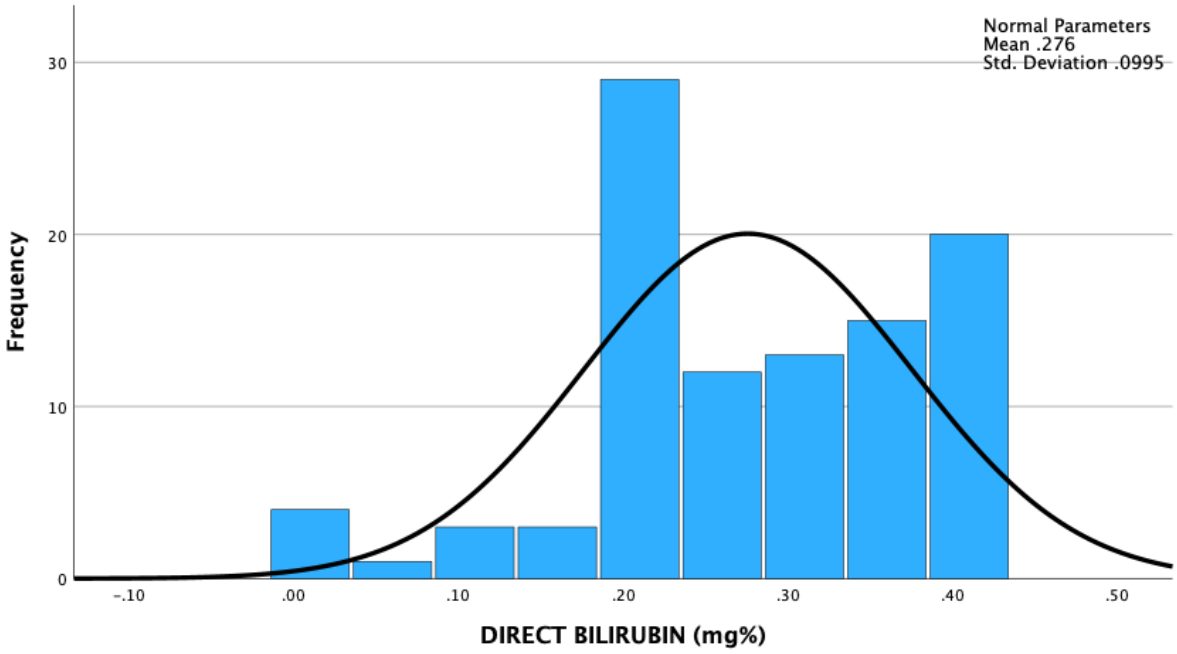
	Number	Mean	SD	Minimum	Maximum	Median
Total Bilirubin (mg%)	100	.7163	.1890	0.3200	1.0800	0.6850



The total bilirubin levels of all the 100 patients in the study where analysed, and the mean total bilirubin level was found to be 0.72mg% and standard deviation is 0.189. The minimum total bilirubin level was found to be 0.32mg% and the maximum was found to be 1.08mg% .The value of p after one-sample Kolmogorov-Smirnov Normal Test is 0.024

Table 25: mean Direct Bilirubin (mg%)

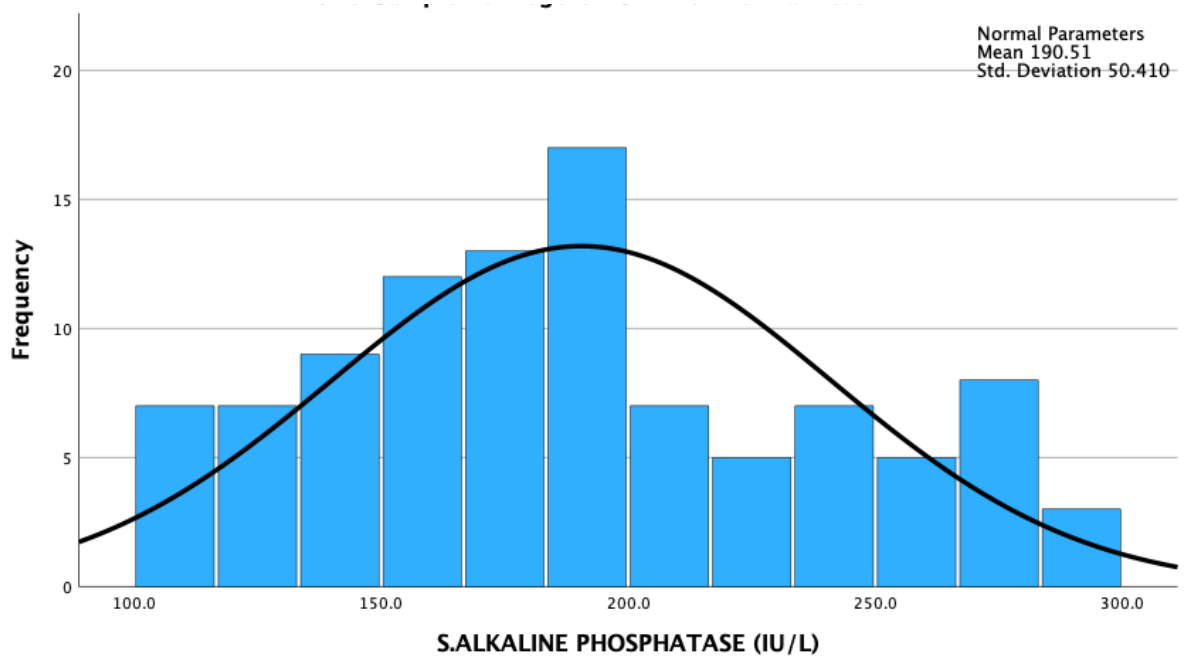
	Number	Mean	SD	Minimum	Maximum	Median
Direct Bilirubin (mg%)	100	.2756	.0995	0.0100	0.4100	0.2700



The direct bilirubin levels of all the 100 patients in the study where analysed, and the mean direct bilirubin level was found to be 0.27mg% and standard deviation is 0.0995. The minimum direct bilirubin level was found to be 0.01mg% and the maximum was found to be 0.41mg% .The value of p after one-sample Kolmogorov-Smirnov Normal Test is 0.025

Table 26:mean Alkaline Phosphatase (IU/L)

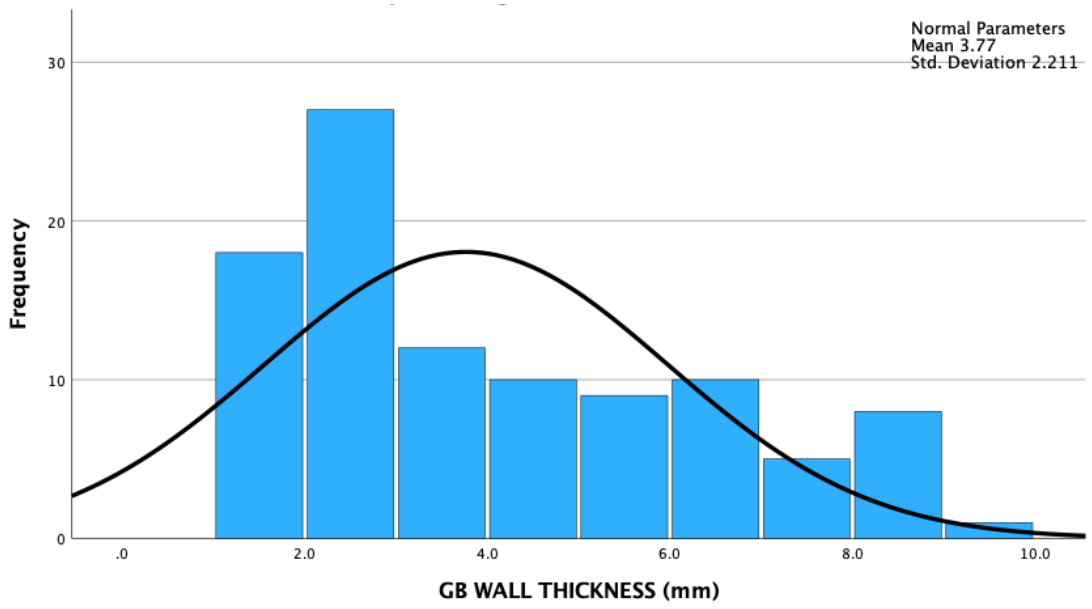
	Number	Mean	SD	Minimum	Maximum	Median
Alkaline Phosphatase (IU/L)	100	190.5120	50.4096	104.2000	297.0000	186.0000



The serum alkaline phosphatase levels of all the 100 patients in the study where analysed, and the mean serum alkaline phosphatase level was found to be 190.51IU/L, and standard deviation is 50.40. The minimum serum alkaline phosphatase level was found to be 104.2IU/L and the maximum was found to be 297IU/L .The value of p after one-sample Kolmogorov-Smirnov Normal Test is 0.049

Table 27: mean Gb Wall Thickness (mm)

	Number	Mean	SD	Minimum	Maximum	Median
Gb Wall Thickness (mm)	100	3.7660	2.2107	1.0000	9.0000	3.0000



The gall bladder specimen post laparoscopic/open cholecystectomy of all the 100 patients in the study where sent for histopathological examination and the gall bladder wall thickness was analysed, and the mean gall bladder wall thickness was found to be 3.77mm and standard deviation is 2.21. The minimum gall bladder wall thickness was found to be 1mm and the maximum gall bladder wall thickness was found to be 9mm. The value of p after one-sample Kolmogorov-Smirnov Normal Test is <0.001.

DISCUSSION AND CONCLUSION

DISCUSSION

In our study, prospective analysis of all the patients with chronic calculus cholecystitis was done on the basis of clinical, radiological and histopathological findings. This study was done over a period of one year. Data analysis was done and compared to other relevant studies after due research and elicited below.

Age incidence:

In our study the maximum patients where found in the age group of 31-40 years – 38 patients (38%). Around 23 patients (23%) where found in the age group of 41-50 years. 22 patients (22%) where found in the age group of 18-30 years. 8 patients (8%) where found in the age group of 51-60 years. 9 patients (9%) where found in the age group 61-75 years. The mean age was found to be 40 years with standard deviation of 12.01. The minimum age in this study is 18 years and the maximum age is 73 years. The median age is 40 years. The p value is 0.04 and considered statistically significant.

In a study by **Selvi T R** et al study maximum patients where found in the age group of 51-60 years , 18 patients (27.69%), around 14 patients (21.5%) where found in the age group of 18-30 years, 10 patients (15.3%) found in the age group of 31- 40 years, 15 patients (23.07%) found in 41-50 years, with mean age of 45.9 years. [64]

In **Siddiqui G F** et al study the maximum patients presenting with chronic calculus cholecystitis was found similar to this study in 31-40 years (27.8%). In the age group of 18-30 years 54 patients where found (24.6%), around 59 patients (26.8%) found in 41-50 years, around 34 patients (15.4%) found in 51-60 years age group, 10 patients (4.5%) found in 61-70 years age group, 2 patients (0.9%) found in 71-80 years of age with mean age of 32.25 years. [47]

In **Nagi. G.S** et al study maximum patients with this pathology where found again in the age group of 31-40 years, 37 patients (35.6%), 8 patients (7.69%) where in the age group of 21-30 years, 31 patients (29.81%) in age group of 41-50 years, 13 patients (12.5%) in age group of 51-60 years, 13 patients (12.5%) in the age group of 61-70 years. [47]

Gender distribution:

In the present study a female preponderance was observed among the study population. 78 patients where found to be females and 22 patients where found to be males. Around 78% where observed to be females and male : female ratio is 1:3.5 .

Similar results where seen in **Selvi T R** et al study with 64.1% of study population (50 patients) being females and 35.89% (28 patients) where male to female ratio being 1:1.8. [64]

In **Siddiqui G F et at** study female constituted to be 87% of the study population. The male to female ratio is 1:7. [47]

In a study done by **Nagi G S et al** 80.7% of the study population where females and male to female ratio 1:4. [65] In study done by **Ezhil A N** et al, the ratio of female to male was found to be 3:1. [43] In study done by **Beena D** et al the male to female ratio is 0.86:1. [67]

In another study done by **Rachamalla R R** et al 66% where females having chronic calculus cholecystitis. [70]

Diet:

In this study the diet pattern of all the patients where assessed and it was found that 86 patients (86%) consumed mixed diet/non vegetarian diet and 14 patients (14%) consumed vegetarian diet. The ratio of mixed diet: vegetarian diet is found to be 6:1.

Chronic calculus cholecystitis is found to be most common in patients consuming mixed diet due to high protein and fat consumption leading to decreased fiber intake leading to increased gall stone formation as seen in **Selvi T R** et al study where the ratio of incidence of this pathology between mixed diet and vegetarian diet was found to be 8:2. [64]

Similar results where found in **Ezhil A et al** study, with ratio being 6:1 and 85% consumed mixed diet and 15% consumed vegetarian diet. [43]

In **Rachamalla R R** et al 's study ratio of mixed diet to vegetarian diet was found to be 2:1 and 68% consumed mixed die and 32% consumed vegetarian diet. [70]

Socio-economic status:

On analysing the socio-economic status, according to modified kuppuswamy scale it was found that, 38 patients (38%) belonged to class II, 36 patients (36%) belonged to class III, 16 patients (16%) belonged to class V, 8 patients (8%) belonged to class IV, 2 patients (2%) belonged to class I. Patients belonging to class II where seen to mostly present with the disease- 38%.

Results seen in **Jain V** et al 's study where 60% of the study population presented with chronic calculus cholecystitis.[48]

Symptoms and signs:

In this study the presenting symptoms of all the patients where noted, and observed that the chief complaint of abdominal pain was present in 73 patients (73%), fever was present in 7 patients (7%) and absent in 93 patients (93%). Nausea and vomiting was present in 21 patients (21%) and absent in 79 patients (79%). Dyspepsia was present in 62 patients (62%) and absent in 38 patients (38%).

In this study the most common symptom was found to be abdominal pain, which was present in 73% of the patients, nausea and vomiting was seen in 21% of the patients, dyspepsia in 62% patients and fever only in 7% of the patients.

On examining the patient's abdominal tenderness was seen in 71 patients (71%) and absent in 29 patients (29%). Palpable mass was felt in right hypochondrial region in 6 patients (6%) and absent in 94 patients (94%).

In the study done by **Selvi T** et al, 66.67% patients (52 patients) where found to have abdominal pain, 13 patients (16.6%) had nausea and 10 patients (12.82%) had vomiting. [64]

In study done by **Siddiqui F G** et al it was found that abdominal pain was the most common symptom found in 91.4% of the patients, dyspepsia was found in 61% patients, nausea and vomiting was seen in 20% of the patients. Palpable mass was elicited in 2.3% of the patients. In study done by **Siddiqui F G** et al 2.3 % of patients had mass which was palpable in the right hypochondrium. [47]

Rachamalla R R study showed that 98% of the patients present with abdominal pain, dyspepsia was seen in 82.1% patients, nausea and vomiting noted in 54.7% of the patients and fever seen in 11% of the patients. Signs of abdominal tenderness was seen in 83.1% of the patients and palpable mass was felt in 15.7% of the patients. [70]

In **Ezhil A N** et al 's study abdominal pain was seen in 55% of the patients (55 patients), which is the most common symptom. [43]

In **Karlati SS et al's** study abdominal pain was seen in 86% of patients (89 patients),which was observed to be the most common symptom. Dyspepsia was seen in 64 patients (60.5%) , nausea and vomiting was seen in 31 patients (29.8%). [66]

In **Mohandas G** et al study abdominal pain was the most common symptom seen in 100% of the patients (50 patients), fever was seen in 23 patients (46%), vomiting was seen in 12 patients (24%).[46]

In **Doshi S R** et al's study abdominal pain was seen in 93.9% of the patients, nausea and vomiting in 35% of patients and fever in 15% of the patients.[60]

Laboratory investigations:

The hemoglobin level of all the patients where assessed and the mean was found to be 12.11g/dl with standard deviation of 1.18. The maximum hemoglobin level is 10.2 g/dl and the minimum hemoglobin level is 16.9 g/dl. The median is 12.10 g/dl. P value is 0.2

The total leukocyte count of all the patients where assessed and the mean total leukocyte count is 7697.31(1000/mm^3) with standard deviation 1341.5, maximum total leukocyte count is 9872(1000/mm^3) and minimum total leukocyte count is 4395(1000/mm^3). The median leukocyte count is 7689(1000/mm^3). The p value is 0.005. In study by **Siddiqui F G** et al, the mean TLC count was found to be 6520(1000/mm^3). [47]

The platelet count of all the patients where assessed and the mean total platelet count is 2.57 (lakh/mm^3) with standard deviation of 0.48(lakh/mm^3). The maximum platelet value is 3.72(lakh/mm^3) and the minimum platelet value is 1.14(lakh/mm^3). The median platelet value is 2.5(lakh/mm^3). The p value is 0.026.

The total bilirubin levels of all the patients where assessed and the mean total bilirubin levels is 0.716mg%, with standard deviation of 0.189mg%. The maximum total bilirubin level is 1.08mg% and the minimum total bilirubin level is 0.32mg%. The median total bilirubin level is 0.685mg%. The p value is 0.024

The direct bilirubin level of the all the patients where assessed and the mean direct bilirubin level is 0.27mg% with standard deviation of 0.995mg%. The maximum direct bilirubin level is 0.41mg% and the minimum direct bilirubin level is 0.01mg%. The median direct bilirubin level is 0.27mg%. The p value is 0.025.

The alkaline phosphatase level of all the patients where assessed and the mean alkaline phosphatase level is 190.51IU/L with standard deviation of 50.41IU/L. The maximum alkaline phosphatase level is 297IU/L and the minimum alkaline phosphatase level is 104.2IU/L. The median alkaline phosphatase level is 186IU/L. The p value is 0.04. Results seen in **Siddiqui F G et al** study also showed results with the mean alkaline phosphatase level is 186.2IU/L.[47]

Ultrasonography findings:

The ultrasound findings of all the patients of chronic calculus calculus cholecystitis was assessed and found that gall bladder thickness was >3mm in 86 patients (86%) and normal in 14 patients (14%) of the patients. The mean was found to be 3.7mm with standard deviation of 2.2mm.

The maximum wall thickness was found to be 9mm and the minimum wall thickness was found to be 1mm. The median is 3mm. The p value is <0.001

Around 74 patients (74%) where found to have small multiple calculi and 26 patients (26%) where found to have large, single calculi. The p value is <0.001

In **Ezhil A N** et al's study it was found that gall baldder thickness >3mm was seen in 57% of the patients during ultrasonography. 80% of the patients where found to have small, multiple calculi and 20% patients had single large calculus.[43]

In **Rachamalla R R** study gall baldder wall thickness was >3mm in 88.4% of patients, small multiple calculi was seen in 60% of the patients and 40% of the patients had large single calculus. [70]

Surgery:

The definitive treatment for chronic calculus cholecystitis is surgical removal of gall bladder, which can be either done laparoscopically (laparoscopic cholecystectomy) or open cholecystectomy. In this study 76 patients (76%) underwent laparoscopic cholecystectomy and 24 patients (24%) underwent open cholecystectomy.

In study by **Rachamalla R R** study 61.5% of the patients underwent laparoscopic cholecystectomy and 38.9% patients underwent open cholecystectomy. [70]

Intra-operative findings:

Intraoperatively, the gall bladder gross morphology was studied and the gall bladder was found to be contracted in 51 patients (51%), found to be elongated in 11 patients (11%) and found to be normal in 38 patients (38%). The p value is <0.001

Adhesions where found in 11 patients (11%) and adhesions where absent in 89 patients (89%). The p value is <0.001. In **Jain V** et al's study intraoperatively adhesions where seen in 9% of the patients. [74]

The calot's triangle anatomy was studied and it was found to be fibrosed in 13 patients (13%) and found to be normal in 87 patients (87%)

In study done by **Jain V et al** 20% of the patients had contracted gall bladder. [74]

Histopathological analysis:

In this study post surgical excision, the gall bladder was sent for histopathological examination. It was found that gall bladder wall thickness was >3mm in 86 patients (86%), and normal in 14 patients (14%). The mean gall bladder wall thickness is 3.7mm with standard deviation

2.2mm. The maximum wall thickness was found to be 9mm and the minimum wall thickness was found to be 1mm. P value is <0.001.

Based on the number of inflammatory cells present 60% of the patients (60 patients) had mild inflammation, moderate inflammation in 24% of the patients (24 patients) and 16% had severe inflammation (16 patients)

The gross specimen of gall bladder was examined and found that 50 patients (50%) had contracted gall bladder, 11 patients (11%) had elongated gall bladder and in 39 patients (39%) of the patients the gall bladder size was found to be normal. The p value was found to be <0.001.

In **Khan M D** et al study it was found that 78.17% had mild inflammation, 9.6% had moderate inflammation and 12.1% had severe inflammation.[68]

In **Ezhil A N** et al's study it was found that gall bladder thickness >3mm was seen in 57% of the patients (57 patients) and <3mm in 43% of the patients(43 patients). [43]

In **Rachamalla R R** study gall bladder wall thickness was >3mm in 88.4% of patient. **[70]**

In **Beena D** et al's study all the cases had inflammation and 144 patients (72%) had mild inflammation and 23 patients (11.5%) had moderate inflammation and 8 patients (4%) had severe inflammation. [65]

In **Khan DM** et al's study it was observed that severe inflammation was seen in 154 cases(78.1%), moderate inflammation was seen in 19 cases(9.64%) and mild inflammation was seen in 24 cases(12.18%).[68]

In **Jain V et al**'s study it was observed that 20% of the patients had contracted gall bladder and 70% of the patients had distended gall bladder. **[74]**

Gall stone analysis:

In this study, post surgical excision of the gall bladder, the gall stones where analyzed and it was found that 58% of the patients (58 patients) had mixed stones, 32% of patients (32 patients) had cholesterol stones, and 10% of the patients (10 patients) had pigment stones.

In **Selvi T R** et al 's study 72% of the patients where found to have pigment stones (47 patients), 15% where found to have cholesterol stones (10 patients) and 12% found to have mixed stones (8 patients). **[64]**

In **Nagi G S** et al's study 80.7% patients where found to have mixed stones, 13.5% where had cholesterol stones and 5.8% had pigment stones.[65]

In **Ezhil A N** et al's study 78% patients (78 patients) had mixed stones, 14% of patients (14 patients) had pigmented stones and 8% had cholesterol stones (8 patients). [43]

In **Karlatti S et al** study 80.7% of the patients had mixed stones (84 patients), 13.5% had cholesterol stones (14 patients) and 5.8% had pigment stones (6 patients).It was found that mixed type of stone is more common. **[66]**

In **Khan DM** et al's study, it was observed that pigmented stones where found to be most common in 93 patients (76.13%), cholesterol stones where found in 17 patients (13.49%) and mixed stones where found in 13 patients (10.31%).[68]

In **Rachamalla R R** et al study 89% of the patients had mixed stones, 9% of the patients had cholesterol stones and 2% of the patients had pigment stones. [70]

CONCLUSION

- In our study it was found that, majority (38%) of the patients patient's were 31-40 years old. Age was statistically significant. It was found that, the mean Age of patients was [40.3600± 12.0181].
- In our study female preponderance was present and is statistically significant.
- It was also seen that most of the patients with chronic calculus cholecystitis consumed mixed diet (86%)
- The most common symptom of the patients where found to be abdominal pain (73%), which was statistically significant, and 71% of the patients had abdominal tenderness on examination.
- When the patients underwent ultrasonography the gall bladder thickness >3mm was found in 86% of the patients, and 74% of the patients had small multiple calculi.
- The definitive treatment of chronic calculus cholecystitis is surgical excision of the gall bladder. 76% of the patients underwent laparoscopic cholecystectomy. Intraoperatively gall bladder was contracted in 51% and adhesions where found in 11%.
- On histopathological analysis, the gall bladder was found to be contracted in 50% of the patient's, and gall bladder wall thickness >3mm was found in 86% of the patients.
- On analysing the gall stones the most common type of stones where found to be mixed stones (89%) in our study.

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PROFORMA

S. No.:

Date:

Name: Age:

Weight: BMI:

MRD No: Occupation:

Address:

Socio-economic status:

Final Diagnosis:

CHIEF COMPLAINTS:

HISTORY:

1. Pain:

   Duration

   Location

   Character

   Radiation

   Aggravating factor

2. Fever:

3.Nausea, Vomiting

4. Dyspepsia

5.Any other complaints:

PAST HISTORY:

Past history of recurrent abdominal pain.

EXAMINATION:

1. General physical examination:

Vitals:

Pulse

Blood pressure

Temperature

Respiratory rate

Pallor: Icterus: Clubbing:

Cyanosis: Oedema: Lymph Nodes:

2. Systemic examination:

Central Nervous System:

Cardiovascular System:

Respiratory System:

Abdomen Examination:

Inspection:

Pain in right hypochondrium

Palpation:

Palpable Gall bladder

Percussion:

Auscultation:

INVESTIGATIONS:

1. Complete blood counts:

   Hb- TLC- Platelets-

   DLC- N L M E B

2. Blood sugar (Random)-
3. Viral Markers:

   HBsAg- HCV-

   HIV 1&2-
4. Liver Function Test:

   S. Bilirubin Total- S. Bilirubin direct-

   S.G.O.T. - S.G.P.T.-

   S. Alkaline Phosphatase-
5. Kidney Function Test:

   Blood Urea- Serum Creatinine-
6. Urine routine and microscopy:

Routine:	Microscopy:
Colour-	RBC/hpf-
pH-	Pus cells/hpf-
Sp. Gravity-	Epithelial cells/hpf-
Protein-	Cast/hpf-
Sugar-	Crystals-
Other-	Other-

7. P.T.- I.N.R-
8. USG Abdomen:

   Gall bladder wall thickness-
   Gall bladder wall edema-
   Number and size of calculous-
   Fluid in Morrison's pouch-
   Impacted stone in hartmann's pouch-
   CBD-
9. Type of Surgery:
10. Intraoperative surgical changes:
11. Histopathological changes:

SANTOSH MEDICAL COLLEGE AND HOSPITAL (GHAZIABAD)

INFORMED CONSENT

I _____ Son/Daughter/Wife of _____ resident of _____.

hereby declare that I give my full, free and voluntary informed consent in the thesis – **Chronic calculus cholecystitis: clinicopathological study with lab-based evidence.**

Dr._____ has informed me to my full satisfaction, in the language I understand, about the purpose, nature of study and various laboratory investigations for the study to be carried out. I have been informed about the duration of the study and instructions to be followed during the study period.

I give full consent for being enrolled in the above study and I reserve my rights to withdraw from this study, whenever I wish without prejudice of my right to undergo further treatment at Santosh Hospital, Ghaziabad U.P.

Patient's/ Patient's relative's signature
Or thumb impression

Doctors signature

Name:

Date:

We have witnessed that the patient signed the above form in the presence of his free will after fully understanding its content.

Signature of Witness

Name

Signature of Investigator
Name: Dr. Janani R G
Designation: PG Department of General Surgery
Contact No.- 9952054869

<u>संतोष मेडिकल कॉलेज एवं अस्पताल (गाजियाबाद)</u>

<u>सहमति पत्र (सूचित)</u>

मैं _____ बेटा / बेटी /पत्नी_____

निवासी _____ घोषणा करता हूं कि मैं डॉ ._____, ने मुझे मेरी भाषा में अपने अध्ययन **Chronic calculus cholecystitis-clinicopathological study with lab based evidence.**

अध्ययन के उद्देश्य के बारे में, और अध्ययन के दौरान अपनाई जाने वाली विभिन्न प्रयोगशाला जांच के बारे में सूचित कर दिया है। मुझे अध्ययनकी अवधि और उसके दौरान अपनाए जाने वाले निर्देश भी मेरी भाषा मे समझा दिए गए हैं| मैं उपरोक्त अध्ययन में बिना किसी दबाव के दाखिला ले रहा हूं और पूर्ण सहमति दे रहा हूं | सन्तोष अस्पताल, गाजियाबाद में अपने आगे के उपचार पर बिना प्रतिकूल प्रभाव डाले इस अध्ययन से और प्रयोगशाला जांच की प्रकृति से मैं जब चाहूँ बाहर जाने के अपने अधिकार को सुरक्षित रख रहा हूं |

रोगी / रोगी के रिश्तेदार के हस्ताक्षर डॉक्टर के हस्ताक्षर

नाम

दिनांक:

मेरी उपस्थिति में मरीज ने पूरी तरह से डाकटर के बताए गए अध्ययन और निर्देशों को समझने के बादअपनी स्वतंत्र इच्छा से ऊपर के फार्म पर हस्ताक्षर किए हैं ।

हस्ताक्षर

नाम: डॉ जननी.आर.जी

पदनाम: पीजी

शल्य चिकित्सा विभाग

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ETHICAL CLEARANCE

SANTOSH
Deemed to be University
(Established u/s 3 of the UGC Act, 1956)

F. No. SU/2021/1830[53] Dated: 17.07.2021

Subject: Grant of Ethical Clearance for Thesis Protocol Topic **"CHRONIC CALCULUS CHOLECYSTITIS : A CLINICOPATHOLOGICAL STUDY WITH LAB BASED EVIDENCE."**, submitted by **Dr. Janani R G,** MD/MS student of Batch 2020-2021, Department of **General Surgery**.

*****

With reference to his/her request for grant of Ethical Clearance for the Thesis Protocol entitled **"CHRONIC CALCULUS CHOLECYSTITIS : A CLINICOPATHOLOGICAL STUDY WITH LAB BASED EVIDENCE."**, **Dr. Janani R G** is informed that the Thesis Protocol submitted by him/her was considered by the **Screening Committee** of the Santosh Medical College & Hospital in its meetings held on 19.03.2021, 22.03.2021, 24.03.2021, 25.03.2021, 26.03.2021, 27.03.2021 and 06.04.2021. The recommendations of the **Screening Committee** were considered in detail by the Institutional **Ethics Committee** in its meeting held on **12.07.2021** and the same was **approved** by the **Ethics Committee**.

He /She is informed accordingly for further necessary action.

[Dr. V. P. Gupta]
REGISTRAR

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PLAGIARISM CERTIFICATE

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TO WHOM IT MAY CONCERN

This is to certify that the statistical analysis component of the dissertation titled **"Chronic calculus cholecystitis: A clinicopathological study with lab-based evidence"** done by Dr. Janani R G, 3rd year post graduate trainee in the Department of General Surgery, Santosh Medical College and Hospital, Ghaziabad, has been conducted under my direct guidance and supervision.

All the statistical calculations of this study are authentic and correct to the best of my knowledge.

Wish her all the success in her life.

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MASTER CHART

S.NO	AGE (yrs)	Age in years	SEX	SOCIO-ECONOMIC STATUS	DIET	ABDOMINAL PAIN	FEVER	NAUSEA & VOMITING	DYSPEPSIA	DURATION(NO. OF MONTHS)	TENDERNESS	PALPABALE MASS	HB(g/dl)	TLC (1000/mm3)	PLATELETS(lakh/mm3)	TOTAL BILIRUBIN (mg%)	DIRECT BILIRUBIN (mg%)	S.ALKALINE PHOSPHATASE (IU/L)	GB WALL THICKNESS	NUMBER AND SIZE OF CALCULI	TYPE OF SURGERY	GALL BLADDER GROSS	ADHESION	CALOT'S ANATOMY	GALL STONE	CALCULI	GALL BLADDER SIZE	GB WALL THICKNESS (mm)	DEGREE OF INFLAMMATION
1	40	2	Female	3	MD	Yes	No	Yes	Yes	36	Yes	No	11.1	6285	3.1	0.82	0.26	211	N	SM	OC	normal	no	normal	M	SM	N	2	MI
2	50	3	Female	2	MD	Yes	No	No	Yes	6	Yes	No	12.1	6215	2.5	0.81	0.19	215	N	SM	LC	normal	no	normal	M	SM	N	2	MI
3	33	2	Female	3	MD	Yes	No	No	Yes	5	Yes	No	11.2	7400	2.42	0.97	0.32	150	T	SM	OC	normal	no	normal	C	SM	N	3	MI
4	47	3	Female	5	MD	Yes	No	Yes	Yes	36	Yes	No	12.4	8170	1.84	0.68	0.24	150	T	SM	OC	contracted	no	normal	P	SM	C	3	MIX
5	27	1	Male	2	MD	Yes	No	No	Yes	6	Yes	No	11.9	5723	2.9	0.97	0.33	179	N	SM	LC	contracted	no	normal	M	SM	C	2	D
6	64	5	Female	5	MD	Yes	No	Yes	Yes	8	Yes	No	11.8	5280	2.4	0.76	0.22	197	N	LS	OC	contracted	no	normal	C	LS	C	2.5	D
7	50	3	Male	3	MD	Yes	No	Yes	Yes	12	Yes	No	12.5	7931	3.1	0.61	0.22	231.1	T	SM	LC	normal	no	normal	M	SM	N	3.5	MI
8	37	2	Female	2	MD	Yes	No	No	No	8	Yes	No	13.1	6321	2.9	0.91	0.28	188	T	LS	LC	normal	no	normal	C	LS	N	3	MI
9	26	1	Female	2	MD	Yes	No	No	Yes	2	Yes	No	12.5	5483	2.34	0.83	0.24	123.6	N	SM	LC	normal	no	normal	C	SM	N	1	MI
10	40	2	Male	2	V	Yes	No	No	No	4	No	No	10.7	7859	2.5	0.9	0.4	234	N	SM	LC	normal	no	normal	C	SM	N	1.7	MI
11	38	2	Female	2	MD	Yes	No	No	Yes	6	Yes	Yes	11.2	8759	2.4	0.98	0.39	143	N	SM	LC	normal	yes	fibrosed	C	SM	N	2	MI
12	43	3	Female	3	MD	Yes	No	No	Yes	7	No	No	12.8	9600	2.56	0.51	0.22	188.6	N	SM	LC	contracted	no	normal	M	SM	C	1.6	MIX
13	40	2	Female	2	MD	No	No	No	No	5	No	No	10.5	6758	2.46	0.34	0.41	178.5	T	LS	LC	contracted	no	normal	M	LS	C	3	MIX
14	61	5	Female	3	MD	Yes	No	No	No	9	Yes	No	12.3	7890	2.76	0.56	0.4	112.3	T	LS	LC	contracted	yes	fibrosed	M	LS	C	4.5	MI
15	45	3	Female	5	MD	Yes	No	No	No	13	Yes	No	13.2	6978	2.56	0.76	0.3	223	T	LS	LC	elongated	no	normal	M	LS	E	7	D
16	50	3	Female	3	MD	No	No	No	No	15	Yes	No	11.4	7568	2.8	0.89	0.33	194	T	LS	LC	elongated	no	normal	M	LS	E	4	MI
17	35	2	Female	2	MD	No	No	No	No	11	No	No	13.2	8960	2.5	0.98	0.23	145	N	LS	LC	contracted	no	normal	M	LS	C	2	MI
18	29	1	Female	3	MD	Yes	No	No	Yes	12	Yes	No	11.4	6500	1.43	1	0.21	111	T	SM	LC	contracted	no	normal	M	SM	C	3	MI
19	45	3	Male	5	MD	Yes	Yes	No	No	6	Yes	No	10.7	8709	1.67	0.99	0.32	126	T	SM	OC	contracted	no	normal	M	SM	E	5	MI
20	50	3	Female	3	V	Yes	Yes	Yes	No	8	Yes	No	13.9	9056	1.87	0.45	0.34	132.5	T	SM	LC	normal	no	normal	M	SM	N	5.5	D
21	34	2	Female	2	MD	No	No	No	No	9	No	No	12.5	6580	2.5	0.54	0.35	166.9	N	SM	LC	normal	no	normal	M	SM	N	2	MI
22	33	2	Male	3	MD	Yes	No	Yes	Yes	6	No	No	11.2	7508	2.65	0.67	0.14	132	N	SM	LC	contracted	no	normal	C	SM	C	1.1	MI
23	55	4	Female	2	MD	No	No	No	Yes	14	Yes	No	10.5	8053	2.34	0.43	0.4	187	N	LS	LC	normal	yes	fibrosed	C	LS	N	1	MI
24	26	1	Female	2	MD	No	No	No	No	15	Yes	No	10.9	5454	2.2	0.45	0.39	197	T	LS	LC	elongated	yes	fibrosed	C	LS	N	5	MIX
25	38	2	Female	2	MD	No	No	No	No	19	Yes	No	10.5	6589	1.53	0.67	0.24	150	T	LS	LC	normal	no	normal	P	LS	N	8	D
26	55	4	Female	2	MD	Yes	No	No	Yes	21	Yes	No	10.9	5200	2.91	0.96	0.02	282	N	SM	LC	elongated	no	normal	M	SM	E	2	MI
27	28	1	Female	2	V	Yes	No	No	No	24	Yes	No	11	7800	1.14	0.65	0.34	272.2	N	LS	LC	contracted	yes	fibrosed	M	LS	C	2	MI
28	32	2	Female	2	MD	Yes	No	No	No	28	Yes	No	14.1	5440	1.56	0.61	0.22	280	T	LS	LC	normal	no	normal	M	LS	N	8	D
29	32	2	Male	2	MD	Yes	No	No	No	12	Yes	No	12.1	6589	2.73	1.08	0.4	295	N	SM	LC	normal	no	normal	M	SM	N	1.8	MI
30	26	1	Female	2	MD	No	Yes	No	Yes	12	No	Yes	11.7	8800	2.53	0.8	0.21	104.2	N	SM	OC	elongated	yes	fibrosed	C	SM	E	1.4	MI
31	49	3	Female	3	MD	No	No	No	Yes	28	Yes	Yes	11.2	7689	1.9	0.56	0.34	123.2	T	SM	LC	contracted	yes	fibrosed	C	SM	C	3.5	MI
32	25	1	Female	5	MD	Yes	No	Yes	No	36	Yes	No	12.2	8945	2.1	0.43	0.25	111.2	N	SM	LC	contracted	no	normal	P	SM	C	2	MI
33	52	4	Female	3	MD	Yes	Yes	No	Yes	4	No	No	11	6879	2.4	0.76	0.33	176.5	T	SM	OC	normal	no	normal	P	SM	N	6	MI
34	28	1	Female	3	MD	Yes	No	No	Yes	6	Yes	No	10.9	5792	2.76	0.67	0.4	195.3	T	SM	LC	contracted	no	normal	M	SM	C	4	MI
35	31	2	Male	3	MD	Yes	No	Yes	Yes	4	No	No	16.9	6600	3.72	1.01	0.02	263	T	LS	LC	normal	no	normal	M	LS	N	3.2	MI
36	68	5	Male	5	MD	Yes	No	No	Yes	12	Yes	No	13.2	6347	2.45	0.97	0.3	211.2	N	LS	LC	elongated	no	normal	M	LS	E	1.9	MI
37	52	4	Male	2	MD	Yes	No	No	Yes	9	Yes	No	13	6360	2.31	0.65	0.36	297	T	SM	LC	contracted	no	normal	M	SM	C	4	MI
38	45	3	Female	5	MD	Yes	No	Yes	Yes	16	Yes	No	12.8	6743	1.94	0.56	0.26	256	T	SM	LC	contracted	yes	fibrosed	M	SM	C	6.2	MIX
39	43	3	Male	3	MD	No	No	No	Yes	13	No	No	14.7	7130	2.76	0.68	0.22	249	N	SM	LC	elongated	no	normal	M	SM	E	2.5	MI
40	25	1	Female	2	MD	Yes	No	Yes	No	9	No	No	13.2	9230	2.51	0.63	0.21	172	N	SM	LC	normal	no	normal	M	SM	N	2	MI
41	30	1	Male	3	MD	Yes	No	No	Yes	24	Yes	Yes	12.1	4395	2.6	0.66	0.21	188.1	N	SM	LC	normal	no	normal	P	SM	N	1.4	MI
42	35	2	Female	2	MD	Yes	No	No	Yes	18	Yes	Yes	13.4	5871	2.9	0.76	0.23	176.6	N	SM	LC	contracted	no	normal	C	SM	C	1	MI
43	27	1	Male	2	MD	Yes	No	No	Yes	16	Yes	Yes	11.6	7842	3.1	0.69	0.22	143.1	T	SM	OC	contracted	no	fibrosed	M	SM	C	7.5	D
44	23	1	Female	2	MD	Yes	No	Yes	No	36	Yes	No	10.4	4420	2.95	0.62	0.19	231	T	SM	LC	contracted	no	normal	M	SM	C	4	MI
45	48	3	Female	2	V	No	No	No	No	23	No	No	12.6	9872	3.2	0.93	0.34	122.1	N	LS	OC	normal	no	normal	C	LS	N	1	MI
46	33	2	Female	3	MD	No	No	No	Yes	12	No	No	14.1	6892	2.9	0.46	0.35	156.2	T	LS	OC	contracted	no	normal	M	LS	C	7	MI
47	40	2	Female	3	MD	No	No	No	Yes	8	No	No	13.2	7842	2.5	0.65	0.39	176.3	N	SM	LC	normal	no	normal	M	SM	N	2.5	MI
48	32	2	Female	2	V	Yes	No	No	Yes	5	No	No	12.2	7321	2.7	0.43	0.4	154.2	N	SM	LC	normal	no	normal	M	SM	N	2	MI
49	46	3	Male	2	V	Yes	No	No	Yes	14	Yes	No	11.1	6593	2.3	0.44	0.4	111.6	T	SM	LC	normal	no	normal	M	SM	N	3.7	MI
50	50	3	Female	2	MD	Yes	No	No	Yes	16	Yes	No	12.6	7865	2.5	0.67	0.22	165.3	N	LS	OC	normal	no	normal	M	LS	N	1.1	MI
51	32	2	Female	5	MD	No	No	Yes	Yes	19	Yes	No	10.4	9832	2.3	0.76	0.25	193.2	N	SM	LC	contracted	no	normal	M	SM	C	2	MI
52	55	4	Female	3	MD	No	No	Yes	Yes	21	Yes	No	11.1	8768	1.9	0.97	0.24	234.2	N	SM	LC	contracted	no	normal	C	SM	C	1.6	MI
53	40	2	Female	2	MD	No	No	No	No	5	Yes	No	10.2	9843	2.4	0.66	0.22	209.3	T	SM	LC	contracted	no	normal	C	SM	C	6	D
54	55	4	Female	2	MD	Yes	No	No	No	3	Yes	No	10.4	8765	3.1	0.39	0.21	283.3	T	SM	LC	contracted	no	normal	C	SM	C	5.3	MI
55	22	1	Male	3	MD	Yes	No	No	No	5	Yes	No	11.4	8976	2.9	0.93	0.12	273.2	T	SM	OC	contracted	no	fibrosed	M	SM	C	8	D
56	27	1	Female	3	MD	Yes	Yes	No	Yes	8	Yes	No	12.5	8745	3.2	0.94	0.14	205.2	T	SM	LC	contracted	no	normal	C	SM	C	5.6	MIX
57	32	2	Female	4	MD	Yes	No	No	Yes	11	Yes	No	13.6	8435	2.4	0.49	0.4	235.5	T	SM	LC	contracted	no	normal	M	SM	C	7.1	D
58	37	2	Female	5	V	Yes	No	No	Yes	17	Yes	No	10.2	9674	2.3	0.9	0.38	204.6	T	SM	LC	contracted	no	normal	C	SM	C	4	MI
59	40	2	Female	3	MD	Yes	No	No	Yes	14	No	No	10.7	8742	2.2	0.85	0.3	199.1	T	SM	LC	contracted	no	normal	M	SM	C	6	MI
60	40	2	Female	2	V	Yes	No	Yes	Yes	4	No	No	11.4	6743	3.2	0.91	0.35	187.3	T	SM	LC	contracted	no	normal	M	SM	C	5.6	MI
61	40	2	Female	4	V	Yes	No	Yes	Yes	6	No	No	11.8	7352	2.8	0.99	0.37	174.3	T	SM	LC	contracted	no	normal	C	SM	C	7	D
62	35	2	Female	1	MD	Yes	No	No	Yes	5	No	No	11.5	9867	3.1	0.56	0.4	155.2	T	LS	LC	contracted	no	normal	C	LS	C	8	D
63	65	5	Female	3	MD	Yes	No	No	Yes	8	Yes	No	12.4	7546	2.9	0.37	0.4	178.2	T	LS	OC	contracted	no	normal	M	LS	C	8	D
64	42	3	Female	2	MD	Yes	No	No	No	12	Yes	No	12.1	8756	1.6	0.74	0.22	254.6	T	LS	LC	normal	no	normal	C	LS	N	8	MIX
65	41	3	Female	3	MD	Yes	No	No	No	6	Yes	No	13.1	7689	2.5	0.54	0.21	244.3	N	SM	LC	normal	no	normal	M	SM	N	4	MI
66	42	3	Female	4	MD	Yes	No	No	No	9	No	No	12.2	6590	2.3	0.95	0.01	234	N	SM	LC	normal	no	normal	M	SM	N	2	MI
67	60	4	Female	5	MD	Yes	No	No	No	12	No	No	11.5	8470	2.1	0.56	0.03	276	T	LS	OC	normal	no	normal	M	LS	N	6	D
68	40	2	Female	5	MD	No	No	Yes	No	11	No	No	12.2	9768	3.2	0.32	0.3	146	N	SM	OC	contracted	yes	fibrosed	M	SM	C	2	MI
69	65	5	Female	3	MD	No	No	No	No	6	No	No	13.2	8702	3.3	0.45	0.4	172	T	SM	OC	contracted	no	normal	M	SM	C	6.5	MIX
70	35	2	Female	2	V	No	No	No	No	9	Yes	No	13.5	7630	3.1	0.78	0.4	154	N	SM	OC	contracted	no	normal	P	SM	C	2	MI
71	44	3	Female	1	MD	No	No	No	Yes	6	Yes	No	12.1	7942	2.9	0.56	0.35	155	N	SM	OC	contracted	no	normal	P	SM	C	2	MI
72	26	1	Female	3	MD	Yes	No	No	Yes	13	Yes	No	11.5	8730	2.7	0.54	0.4	176	T	LS	LC	contracted	no	normal	C	LS	C	9	MIX
73	28	1	Female	3	V	Yes	No	No	Yes	14	Yes	No	11.9	7621	2.5	0.63	0.08	193	N	SM	LC	elongated	yes	fibrosed	C	SM	E	1.7	MI
74	70	5	Male	3	MD	Yes	Yes	Yes	No	8	Yes	No	12.3	6476	2.4	0.67	0.32	113	T	SM	LC	elongated	no	normal	C	SM	E	5	MIX
75	33	2	Female	5	MD	Yes	No	No	No	13	No	No	12.6	8793	2.1	0.78	0.23	143	N	SM	LC	contracted	no	normal	M	SM	C	2	MI
76	52	4	Female	5	MD	Yes	No	No	No	14	No	No	14.2	9658	2.6	0.68	0.34	154	T	LS	OC	contracted	no	normal	M	SM	C	6	MIX
77	50	3	Female	5	MD	Yes	No	No	No	9	Yes	No	11.6	8645	2.9	0.73	0.4	190	N	SM	LC	contracted	no	normal	M	SM	C	2.4	MI
78	27	1	Female	5	MD	Yes	No	No	No	7	No	No	11.7	9768	2.5	0.75	0.22	234	N	SM	LC	contracted	no	normal	C	SM	C	2	MI
79	40	2	Female	4	MD	Yes	No	No	Yes	6	Yes	No	12.4	8642	3.2	0.64	0.21	267	T	SM	OC	normal	no	normal	P	SM	N	5	MIX
80	48	3	Male	3	MD	Yes	No	Yes	Yes	9	Yes	No	10.3	7653	3.3	0.55	0.25	282	N	SM	OC	contracted	no	normal	M	SM	C	4	MIX
81	30	1	Male	4	MD	Yes	No	No	Yes	12	Yes	No	10.5	8121	2.5	0.93	0.38	186	T	SM	LC	normal	no	normal	M	SM	N	5	MIX
82	40	2	Male	2	MD	Yes	No	No	Yes	14	Yes	No	11.3	5721	2.1	0.91	0.37	184	T	SM	LC	contracted	no	normal	M	SM	C	8	MIX
83	25	1	Female	3	MD	Yes	No	No	Yes	18	No	No	12.4	9842	2.4	0.56	0.26	114	N	SM	LC	normal	no	normal	M	SM	N	1.5	MIX
84	35	2	Female	2	MD	Yes	No	No	Yes	16	No	No	13.2	7689	2.5	0.54	0.21	154	N	SM	LC	contracted	no	normal	C	SM	C	1.9	MIX
85	62	5	Female	2	MD	No	No	No	Yes	12	Yes	No	12.3	9265	2.9	0.67	0.19	165	N	SM	OC	contracted	no	normal	C	SM	C	2	MIX
86	38	2	Male	3	V	No	No	Yes	Yes	11	Yes	No	12.6	8790	3.1	0.97	0.14	118	T	SM	LC	contracted	no	normal	C	SM	C	4	MIX
87	73	5	Male	3	MD	No	No	Yes	Yes	16	Yes	No	13.2	7577	3.3	0.87	0.3	210	T	SM	LC	contracted	no	normal	M	SM	C	3	MIX
88	50	3	Female	2	MD	No	No	No	Yes	9	Yes	No	13.7	9786	2.5	0.56	0.38	232	T	LS	LC	contracted	no	normal	M	LS	C	6	MIX
89	32	2	Female	3	MD	Yes	No	No	Yes	5	Yes	No	14.5	7685	2.4	0.86	0.4	265	T	SM	LC	normal	no	normal	M	SM	N	3	MI
90	36	2	Female	4	MD	Yes	No	No	Yes	8	Yes	No	12.3	7685	2.4	0.94	0.22	167	T	SM	LC	normal	no	normal	C	SM	N	3	MI
91	35	2	Female	5	V	Yes	No	No	Yes	7	Yes	No	13.2	6589	2.1	0.86	0.21	166	N	LS	LC	normal	no	normal	C	LS	N	2	MI
92	35	2	Female	4	MD	Yes	No	No	Yes	9	Yes	No	10.6	6673	2.2	0.76	0.28	154.4	T	SM	OC	normal	no	normal	P	SM	N	4	MIX
93	48	3	Female	3	MD	Yes	No	No	Yes	3	Yes	No	11.6	8756	2.9	0.56	0.4	154.2	N	SM	LC	elongated	yes	fibrosed	M	SM	E	1.4	MI
94	42	3	Female	2	V	Yes	Yes	No	Yes	8	Yes	No	12.4	9243	3.2	0.46	0.23	232.2	N	SM	LC	elongated	no	normal	M	SM	E	1.9	MI
95	26	1	Female	4	MD	Yes	No	No	No	9	Yes	No	11.9	7687	3.5	0.87	0.32	265	N	SM	LC	contracted	no	normal	P	SM	C	2	MI
96	25	1	Female	3	MD	Yes	No	Yes	No	12	Yes	No	10.4	5645	3.6	0.94	0.12	284	N	SM	LC	contracted	no	normal	C	SM	C	2	MI
97	62	5	Male	3	MD	No	No	No	No	14	Yes	No	12.1	8798	3.1.	0.76	0.2	186	T	SM	OC	normal	no	normal	C	SM	N	8	D
98	38	2	Female	2	MD	No	No	No	No	8	Yes	No	13.1	7687	2.6	0.85	0.3	143.4	T	SM	LC	normal	no	normal	M	SM	N	6	D
99	18	1	Female	3	MD	No	No	No	Yes	6	Yes	No	13.6	8798	2.5	0.88	0.11	176.5	T	SM	LC	Normal	no	normal	M	SM	N	6	MIX
100	32	2	Male	2	MD	Yes	No	No	Yes	3	No	No	12.1	6787	2.7	0.48	0.19	196.2	N	LS	LC	normal	no	normal	M	LS	N	2	MIX

ABBREVIATIONS

KEY	
SM	Small multiple
LS	Large single
OC	open cholecystectomy
LC	Laparoscopic cholecystectomy
1	upper class
2	upper middle
3	lower middle
4	upper lower
5	lower
V	Veg
MD	mixed diet
C	Cholesterol
P	Pigmented
M	Mixed
C	Contracted
N	Normal
E	Enlarged
MI	Mild
MIX	Mixed
D	Dense
T	Thick